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Detailed Description

Detailed Description

... electrophoretically separating the dispersed carbon nanotubes. Although the additional separation step typically occurs after the nanoparticles are prepared, it is possible that separation may also occur prior to dispersion, during dispersion...onto the nanotubes, a change in the current-voltage (I-V) curve is used to detect the presence of a targeted analyte.

101211 Avarietyofanalytescanbedetectedusingthissensor,includinghydrogen (i.e., protons), ammonia, amine groups, CO and CO2. Nanotubes with amine surface groups arising from the surfactants or...

4/3,KWIC/30 (Item 13 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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01016548 **Image available**

THE USE OF 1D SEMICONDUCTOR MATERIALS AS CHEMICAL SENSING MATERIALS,
PRODUCED AND OPERATED CLOSE TO ROOM TEMPERATURE

UTILISATION DE MATERIAUX SEMI-CONDUCTEURS UNIDIMENSIONNELS COMME MATERIAUX
DE DETECTION CHIMIQUE, PRODUITS ET EXPLOITES A UNE TEMPERATURE PROCHE
DE LA TEMPERATURE AMBIANTE

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DE, DE (Residence), FR (Nationality), (Designated only for: US)

DOCUMENT-IDENTIFIER: US RE30803 E

TITLE: Colorless recording paper

Detailed Description Text (11):

A 2% solution of the hydrazoic acid salt of Michler's Hydrol in dioctyl phthalate is prepared; and this is emulsified in a 20% aqueous solution of polyvinyl alcohol containing a few drops of ammonia, using 2.5 parts by weight of dioctyl phthalate to one part by weight of solid polyvinyl alcohol. The resultant emulsion is coated onto a paper web by standard coating procedures and air-dried to give a substantially colorless transfer sheet. When the coated side is placed in contact with an unfired kaolin-coated paper, pressure applied to the upper side transfers the recording fluid to the kaolin-coated receiving sheet to give a deep blue print which is not discharged by water.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

PGPUB-DOCUMENT-NUMBER: 20050085739
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DOCUMENT-IDENTIFIER: US 20050085739 A1

TITLE: Visual indicating device for bad breath

PUBLICATION-DATE: April 21, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
MacDonald, John Gavin	Decatur	GA	US
Huang, Yanbin	Roswell	GA	US
McGrath, Kevin Peter	Alpharetta	GA	US
Boga, RameshBabu	Roswell	GA	US

US-CL-CURRENT: 600/530

CLAIMS:

1-22. (canceled)

23. A breath testing device comprising nanoparticles and a visual indicating agent that is color sensitive to at least one odorous compound present in the breath of a user.

24. The breath testing device of claim 23, wherein the odorous compound contains sulfur.

25. The breath testing device of claim 23, wherein the odorous compound contains an amine.

26. The breath testing device of claim 23, wherein the visual indicating agent contains a dye having the general formula (I) or (11): $\text{8where, R is H, (NH.sub.2)C.sub.6H.sub.5--}, \text{ or C.sub.6H.sub.5--}; \text{ R' is (CH.sub.3).sub.2NC.sub.6H.sub.5--}, \text{ (NH.sub.2)C.sub.6H.sub.5--}, \text{ (CH.sub.3)C.sub.10H.sub.6(OH)--}, \text{ or (NaCO.sub.2)(CH.sub.3)C.sub.10H.sub.5- (OH)--}; \text{ and R'' is (CH.sub.3).sub.2NC.sub.6H.sub.5--}, \text{ (NH.sub.2)C.sub.6H.sub.5--}, \text{ (CH.sub.2)C.sub.10H.sub.6O--}, \text{ or (NaCO.sub.2)(CH.sub.2)C.sub.10H.sub.5O--};$

27. The breath testing device of claim 23, wherein the visual indicating agent contains pararosaniline base, alpha-naphtholbenzein, naphthochrome green, or combinations thereof.

28. The breath testing device of claim 23, wherein the visual indicating agent contains 4,4'-bis (dimethylamino)-benzhydrol.

29. The breath testing device of claim 23, wherein the nanoparticles have an average size of less than about 100 nanometers.

30. The breath testing device of claim 23, wherein the nanoparticles have an average size of from about 1 to about 50 nanometers.

31. The breath testing device of claim 23, wherein the nanoparticles have a surface area of from about 50 to about 1000 square meters per gram.

32. The breath testing device of claim 23, wherein the nanoparticles have an average size of from about 100 to about 600 square meters per gram.
33. The breath testing device of claim 23, wherein the nanoparticles include silica, alumina, or combinations thereof.
34. The breath testing device of claim 23, wherein the visual indicating agent is contained on a substrate.
35. The breath testing device of claim 34, wherein the substrate contains a fibrous material.
36. The breath testing device of claim 35, wherein the fibrous material contains cellulosic fibers.
37. The breath testing device of claim 34, wherein the substrate is located within a passage of a carrier portion.
38. The breath testing device of claim 34, wherein the substrate covers an end of a carrier portion.
39. The breath testing device of claim 34, wherein the visual indicating agent is applied to the substrate as a solution.
40. The breath testing device of claim 39, wherein the concentration of the visual indicating agent is from about 0.001 to about 15% wt/wt.
41. The breath testing device of claim 39, wherein the concentration of the visual indicating agent is from about 0.005 to about 2% wt/wt.
42. The breath testing device of claim 23, further comprising a zone having a reference color, the reference color being the color to which the indicating agent will change upon exposure to the odorous compound.
43. A dispenser containing the breath testing device of claim 1.
44. The dispenser of claim 43, further comprising at least one breath freshener.
45. The dispenser of claim 44, wherein the breath testing device and breath freshener are contained in different compartments of the dispenser.
46. A breath testing device comprising a carrier portion defining a passage that is open at least one end, wherein the device contains nanoparticles and a visual indicating agent that is color sensitive to at least one odorous compound present in the breath of a user.
47. The breath testing device of claim 46, wherein the carrier portion is a cylindrical structure.
48. The breath testing device of claim 46, wherein the carrier portion is substantially flattened.
49. A method for testing for bad breath in a user, the method comprising: causing the user to blow or breathe onto or into a carrier portion of a breath testing device, the breath testing device containing nanoparticles and a visual indicating agent that is sensitive to at least one odorous compound; and observing whether the visual indicating agent changes color.

L11: Entry 4 of 19

File: PGPB

May 26, 2005

PGPUB-DOCUMENT-NUMBER: 20050112085
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050112085 A1

TITLE: Odor controlling article including a visual indicating device for monitoring odor absorption

PUBLICATION-DATE: May 26, 2005

INVENTOR-INFORMATION:

10/687,269

NAME	CITY	STATE	COUNTRY
MacDonald, John Gavin	Decatur	GA	US
Boga, RameshBabu	Roswell	GA	US
Kim, Jaeho	Roswell	GA	US
Do, Bao Trong	Decatur	GA	US
Kuznetsov, Irene	Lawrenceville	GA	US

US-CL-CURRENT: 424/76.1

CLAIMS:

What is claimed is:

1. An article for controlling odor, the article comprising at least one visual indicating agent that is color sensitive to the odor.
2. The article of claim 1, which further comprises an odor absorbing agent.
3. The article of claim 1, wherein the visual indicating agent is also an odor absorbing agent.
4. The article of claim 1, wherein the indicating agent indicates when the article has been exposed to sufficient odor to saturate the article.
5. The article of claim 1, wherein the indicating agent is located on an indicating device wherein said device is selected from the group consisting of discs, patches and strips, which is applied to or inserted into the article.
6. The article of claim 1, wherein the indicating agent is printed in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
7. The article of claim 1, wherein the indicating agent is coated in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
8. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has not been utilized.
9. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or

more zones to indicate how much of the odor absorbing capacity of the article has been used.

10. The article of claim 1, wherein the odor is selected from the group consisting of body odor, foot odor, urinary odor, tobacco odor, meat odor, garbage odor, basement odor, mercaptans, sulfide, hydrogen sulfide, amines, ammonia, sulfur, sulfur degradation products, aliphatic acids, isovaleric acid, butyric acid and acetic acid.

11. The article of claim 1, wherein the visual indicating agent is selected from the group consisting of neutral red, 3-nitrophenol, Brilliant Yellow, chlorophenol red, Rose Bengal dye, D&C Red 28 dye, 4,4'-bis(dimethylamino)-benzhydrol (BDMD or Michler's hydrol), parosaniline base, alpha-naphtholbenzene, naphthochrome green, methyl red, methyl violet, methyl orange, bromocresol mauve, Acid Blue 80, blue dye Calcocid Blue 2G, ethyl red, bromophenol blue, bromocresol green, crystal violet, cresol red, thymol blue, erythrosine B, 2,4-dinitrophenol, alizarin, bromothymol blue, phenol red, m-nitrophenol, o-cresolphthalein, thymolphthalein, alizarin Yellow Reller, cobalt salts and complexes, copper salts and complexes, copper phenanthroline complexes and iron salts and complexes.

12. The article of claim 11, wherein the visual indicating agent is 4,4'-bis(dimethylamino)-benzhydrol.

13. The article of claim 3, wherein both the odor absorbing agent and visual indicating agent are 4,4'-bis(dimethylamino)-benzhydrol.

14. The article of claim 1, which is selected from a disposable odor absorbing sheet, diaper, undergarment pad, face mask, filtration device, sanitary napkin, tampon, panty shield and incontinence pad.

15. An article for controlling odor comprising a nanoparticle selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold, zinc oxide, copper oxide, and combinations thereof, having thereon at least one metal ion selected from the group consisting of copper ion, silver ion, gold ion, permanganate ion, chlorite ion, persulfate ion, iron ion, and combinations thereof.

16. A visual indicating device for indicating the ability of an odor absorbing article to absorb odor, which includes at least one zone of a visual indicating agent that changes color when exposed to the odor, said zone having a concentration of the visual indicating agent that changes color to indicate that the article is saturated and should be replaced.

17. A method for visually indicating when an article for controlling odor is saturated comprising the steps of: introducing into or onto the article a visual indicating agent that is color sensitive to the odor, and observing the change in color of the indicating agent when the article is saturated with the odor.

18. The use of a visual indicating agent on an article for controlling odor, which provides an indication of when the article is saturated with the odor.

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DOCUMENT-IDENTIFIER: US 20050112085 A1

TITLE: Odor controlling article including a visual indicating device for monitoring odor absorption.

PUBLICATION-DATE: May 26, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
MacDonald, John Gavin	Decatur	GA	US
Boga, RameshBabu	Roswell	GA	US
Kim, Jaeho	Roswell	GA	US
Do, Bao Trong	Decatur	GA	US
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different inventing entity

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
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← same assignee

APPL-NO: 10/687269 [PALM]
DATE FILED: October 16, 2003

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INT-CL-PUBLISHED: [07] A61 L 9/01

US-CL-PUBLISHED: 424/076.1

US-CL-CURRENT: 424/76.1

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The present invention relates to a visual indicating device and an article for controlling odors, in particular foot, garbage, basement, cooking, pet, tobacco, feces and urine odors. The article comprises a visual indicating agent that is color sensitive to the odor, and optionally, an odor absorbing agent. The visual indicating agent changes color when the article has been exposed to a sufficient amount of odor to saturate the article. The indicating agent may be applied in differing concentrations to two or more zones so as to indicate to a user of the article how much of the odor absorbing capacity has been used, or conversely, how much of the odor absorbing capacity remains. Suitable visual indicating agents that change color in response to odors are also described. The article for controlling odors may be a disposable odor absorbing sheet, air freshening product, diaper, undergarment pad, face mask, air filtration device, sanitary napkin, tampon, panty shield or incontinence pad.

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Do, Bao Trong	Decatur	GA	US
Kuznetsov, Irene	Lawrenceville	GA	US

US-CL-CURRENT: 424/76.1

CLAIMS:

What is claimed is:

1. An article for controlling odor, the article comprising at least one visual indicating agent that is color sensitive to the odor.
2. The article of claim 1, which further comprises an odor absorbing agent.
3. The article of claim 1, wherein the visual indicating agent is also an odor absorbing agent.
4. The article of claim 1, wherein the indicating agent indicates when the article has been exposed to sufficient odor to saturate the article.
5. The article of claim 1, wherein the indicating agent is located on an indicating device wherein said device is selected from the group consisting of discs, patches and strips, which is applied to or inserted into the article.
6. The article of claim 1, wherein the indicating agent is printed in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
7. The article of claim 1, wherein the indicating agent is coated in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
8. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has not been utilized.
9. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has been used.

10. The article of claim 1, wherein the odor is selected from the group consisting of body odor, foot odor, urinary odor, tobacco odor, meat odor, garbage odor, basement odor, mercaptans, sulfide, hydrogen sulfide, amines, ammonia, sulfur, sulfur degradation products, aliphatic acids, isovaleric acid, butyric acid and acetic acid.
11. The article of claim 1, wherein the visual indicating agent is selected from the group consisting of neutral red, 3-nitrophenol, Brilliant Yellow, chlorophenol red, Rose Bengal dye, D&C Red 28 dye, 4,4'-bis(dimethylamino)-benzhydrol (BDMD or Michler's hydrol), parosaniline base, alpha-naphtholbenzene, naphthochrome green, methyl red, methyl violet, methyl orange, bromocresol mauve, Acid Blue 80, blue dye Calcocid Blue 2G, ethyl red, bromophenol blue, bromocresol green, crystal violet, cresol red, thymol blue, erythrosine B, 2,4-dinitrophenol, alizarin, bromothymol blue, phenol red, m-nitrophenol, o-cresolphthalein, thymolphthalein, alizarin Yellow Reller, cobalt salts and complexes, copper salts and complexes, copper phenanthroline complexes and iron salts and complexes.
12. The article of claim 11, wherein the visual indicating agent is 4,4'-bis(dimethylamino)-benzhydrol.
13. The article of claim 3, wherein both the odor absorbing agent and visual indicating agent are 4,4'-bis(dimethylamino)-benzhydrol.
14. The article of claim 1, which is selected from a disposable odor absorbing sheet, diaper, undergarment pad, face mask, filtration device, sanitary napkin, tampon, panty shield and incontinence pad.
15. An article for controlling odor comprising a nanoparticle selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold, zinc oxide, copper oxide, and combinations thereof, having thereon at least one metal ion selected from the group consisting of copper ion, silver ion, gold ion, permanganate ion, chlorite ion, persulfate ion, iron ion, and combinations thereof.
16. A visual indicating device for indicating the ability of an odor absorbing article to absorb odor, which includes at least one zone of a visual indicating agent that changes color when exposed to the odor, said zone having a concentration of the visual indicating agent that changes color to indicate that the article is saturated and should be replaced.
17. A method for visually indicating when an article for controlling odor is saturated comprising the steps of: introducing into or onto the article a visual indicating agent that is color sensitive to the odor, and observing the change in color of the indicating agent when the article is saturated with the odor.
18. The use of a visual indicating agent on an article for controlling odor, which provides an indication of when the article is saturated with the odor.

[First Hit](#) [Previous Doc](#) [Next Doc](#) [Go to Doc#](#)



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L2: Entry 1 of 42

File: PGPB

May 26, 2005

DOCUMENT-IDENTIFIER: US 20050112085 A1

TITLE: Odor controlling article including a visual indicating device for monitoring odor absorption

Summary of Invention Paragraph:

[0018] In some instances, the visual indicating agent and odor absorbing agent may be the same agent. For example, BDMB may be used as both the odor absorbing agent and the visual indicating agent for sulfur, amine and ammonia odors.

Summary of Invention - Table CWU:

1TABLE 1 Indicating agents having the general formula (I) or (II) Indicating Agent R R' R" Indicating Agent for Michler's Hydrol H (CH.sub.3).sub.2NC.sub.6H.sub.5-- (CH.sub.3).sub.2NC.sub.6H.sub.5-- Thiols, Mercaptans, (MH) Ammonia, Amines, Diamines and Polyamines Pararosaniline (NH.sub.2)C.sub.6H.sub.5-- (NH.sub.2)C.sub.6H.sub.5-- (NH.sub.2)C.sub.6H.sub.5-- Ammonia, Amines, Base (PAB) Diamines and Polyamines Alpha- naphtholbenzene (ANB) C.sub.6H.sub.5-- 2 3 Ammonia, Amines, Diamines and Polyamines Naphthochrome Green (NCG) C.sub.6H.sub.5-- 4 5 Ammonia, Amines, Diamines and Polyamines

Brief Description of Drawings Paragraph:

[0025] FIG. 2 shows a standard curve for the detection of ammonia by BDMB;

Detail Description Paragraph:

[0066] As shown in FIG. 2, a standard curve was derived using ammonium hydroxide solution as an ammonia odor source detected by BDMB (MH-dye). In FIG. 2 the x-axis is the concentration of ammonia in ppb from 0 to 400 and the y-axis is the absorbance at 590 nm. Into each of 8 vials, 50 .mu.l of a specific concentration of ammonia solution (0, 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, and 0.64%, respectively) was mixed with 150 .mu.l of MH solution (20 .mu.l of 10.0 mg/ml MH in CH.sub.3CN with 5.0 ml of 40 mM sodium acetate and 4 M guanidine HCl, pH 5.1), all available from Aldridge Chem. Co. of Milwaukee, Wis. and the vials were sealed and incubated for less than 4 min.

Detail Description Paragraph:

[0081] It was therefore concluded that BDMB is an effective, multi-functional odor reducing agent for sulfur, amine and ammonia odors which are major components of, among others, urine, feces, dog and cooking odors.

Detail Description Table CWU:

3TABLE 3 Visual indicating agents and the specific odors that cause color change Visual Indicating Agent Odor or Odor Class Michler's Hydrol Ammonia, amines, sulfur compounds Copper salts and complexes Ammonia, amines, sulfur compounds Rose Bengal (Acid Red 94) Sulfur compounds D&C Red 28 (Acid Red 92) Sulfur compounds Cobalt salts and complexes Sulfur compounds, aldehydes, amines Copper phenanthroline Sulfur compounds and amines Iron salts and complexes Sulfur compounds and amines Phenol red Aliphatic carboxylic acids Cresol red Aliphatic carboxylic acids Neutral red Aliphatic carboxylic acids 3-Nitrophenol Aliphatic carboxylic acids Brilliant Yellow Aliphatic carboxylic acids Bromothymol blue Aliphatic carboxylic acids Chlorophenol red Aliphatic carboxylic acids Pararosaniline base Ammonia and amines Alpha-naphtholbenzene Ammonia and amines Naphthochrome green Ammonia and amines

[Previous Doc](#)

[Next Doc](#)

[Go to Doc#](#)

PGPUB-DOCUMENT-NUMBER: 20050112085
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TITLE: Odor controlling article including a visual indicating device for monitoring odor absorption

PUBLICATION-DATE: May 26, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
MacDonald, John Gavin	Decatur	GA	US
Boga, RameshBabu	Roswell	GA	US
Kim, Jaeho	Roswell	GA	US
Do, Bao Trong	Decatur	GA	US
Kuznetsov, Irene	Lawrenceville	GA	US

US-CL-CURRENT: 424/76.1

CLAIMS:

What is claimed is:

1. An article for controlling odor, the article comprising at least one visual indicating agent that is color sensitive to the odor.
2. The article of claim 1, which further comprises an odor absorbing agent.
3. The article of claim 1, wherein the visual indicating agent is also an odor absorbing agent.
4. The article of claim 1, wherein the indicating agent indicates when the article has been exposed to sufficient odor to saturate the article.
5. The article of claim 1, wherein the indicating agent is located on an indicating device wherein said device is selected from the group consisting of discs, patches and strips, which is applied to or inserted into the article.
6. The article of claim 1, wherein the indicating agent is printed in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
7. The article of claim 1, wherein the indicating agent is coated in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.
8. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has not been utilized.
9. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has been used.

10. The article of claim 1, wherein the odor is selected from the group consisting of body odor, foot odor, urinary odor, tobacco odor, meat odor, garbage odor, basement odor, mercaptans, sulfide, hydrogen sulfide, amines, ammonia, sulfur, sulfur degradation products, aliphatic acids, isovaleric acid, butyric acid and acetic acid.

11. The article of claim 1, wherein the visual indicating agent is selected from the group consisting of neutral red, 3-nitrophenol, Brilliant Yellow, chlorophenol red, Rose Bengal dye, D&C Red 28 dye, 4,4'-bis(dimethylamino)-benzhydrol (BDMD or Michler's hydrol), parosaniline base, alpha-naphtholbenzene, naphthochrome green, methyl red, methyl violet, methyl orange, bromocresol mauve, Acid Blue 80, blue dye Calcocid Blue 2G, ethyl red, bromophenol blue, bromocresol green, crystal violet, cresol red, thymol blue, erythrosine B, 2,4-dinitrophenol, alizarin, bromothymol blue, phenol red, m-nitrophenol, o-cresolphthalein, thymolphthalein, alizarin Yellow Reller, cobalt salts and complexes, copper salts and complexes, copper phenanthroline complexes and iron salts and complexes.

12. The article of claim 11, wherein the visual indicating agent is 4,4'-bis(dimethylamino)-benzhydrol.

13. The article of claim 3, wherein both the odor absorbing agent and visual indicating agent are 4,4'-bis(dimethylamino)-benzhydrol.

14. The article of claim 1, which is selected from a disposable odor absorbing sheet, diaper, undergarment pad, face mask, filtration device, sanitary napkin, tampon, panty shield and incontinence pad.

15. An article for controlling odor comprising a nanoparticle selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold, zinc oxide, copper oxide, and combinations thereof, having thereon at least one metal ion selected from the group consisting of copper ion, silver ion, gold ion, permanganate ion, chlorite ion, persulfate ion, iron ion, and combinations thereof.

16. A visual indicating device for indicating the ability of an odor absorbing article to absorb odor, which includes at least one zone of a visual indicating agent that changes color when exposed to the odor, said zone having a concentration of the visual indicating agent that changes color to indicate that the article is saturated and should be replaced.

17. A method for visually indicating when an article for controlling odor is saturated comprising the steps of: introducing into or onto the article a visual indicating agent that is color sensitive to the odor, and observing the change in color of the indicating agent when the article is saturated with the odor.

18. The use of a visual indicating agent on an article for controlling odor, which provides an indication of when the article is saturated with the odor.

[Previous Doc](#)

[Next Doc](#)

[Go to Doc#](#)

apparent to those skilled in the art that various alterations, modifications and other changes may be made to the invention without departing from the spirit and scope of the present invention. It is therefore intended that the claims cover or encompass all such modifications, alterations and/or changes.

What is claimed is:

1. An article for controlling odor, the article comprising at least one visual indicating agent that is color sensitive to the odor.

2. The article of claim 1, which further comprises an odor absorbing agent.

3. The article of claim 1, wherein the visual indicating agent is also an odor absorbing agent.

4. The article of claim 1, wherein the indicating agent indicates when the article has been exposed to sufficient odor to saturate the article.

5. The article of claim 1, wherein the indicating agent is located on an indicating device wherein said device is selected from the group consisting of discs, patches and strips, which is applied to or inserted into the article.

6. The article of claim 1, wherein the indicating agent is printed in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.

7. The article of claim 1, wherein the indicating agent is coated in solution onto the article and allowed to dry so that the dried residue of the solution remains on the article.

8. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has not been utilized.

9. The article of claim 1, wherein the indicating agent is applied in differing concentrations in two or more zones to indicate how much of the odor absorbing capacity of the article has been used.

10. The article of claim 1, wherein the odor is selected from the group consisting of body odor, foot odor, urinary odor, tobacco odor, meat odor, garbage odor, basement odor, mercaptans, sulfide, hydrogen sulfide, amines, ammonia, sulfur, sulfur degradation products, aliphatic acids, isovaleric acid, butyric acid and acetic acid.

11. The article of claim 1, wherein the visual indicating agent is selected from the group consisting of neutral red, 3-nitrophenol, Brilliant Yellow, chlorophenol red, Rose Bengal dye, D&C Red 28 dye, 4,4'-bis(dimethylamino)-benzhy-

drol (BDMD or Michler's hydrol), pararosaniline base, alpha-naphtholbenzene, naphthochrome green, methyl red, methyl violet, methyl orange, bromocresol mauve, Acid Blue 80, blue dye Calcoicid Blue 2G, ethyl red, bromophenol blue, bromocresol green, crystal violet, cresol red, thymol blue, erythrosine B, 2,4-dinitrophenol, alizarin, bromothymol blue, phenol red, m-nitrophenol, o-cresolphthalein, thymolphthalein, alizarin Yellow Reller, cobalt salts and complexes, copper salts and complexes, copper phenanthroline complexes and iron salts and complexes.

12. The article of claim 11, wherein the visual indicating agent is 4,4'-bis(dimethylamino)-benzhydrol.

13. The article of claim 3, wherein both the odor absorbing agent and visual indicating agent are 4,4'-bis(dimethylamino)-benzhydrol.

14. The article of claim 1, which is selected from a disposable odor absorbing sheet, diaper, undergarment pad, face mask, filtration device, sanitary napkin, tampon, panty shield and incontinence pad.

15. An article for controlling odor comprising a nanoparticle selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold, zinc oxide, copper oxide, and combinations thereof, having thereon at least one metal ion selected from the group consisting of copper ion, silver ion, gold ion, permanganate ion, chlorite ion, persulfate ion, iron ion, and combinations thereof.

16. A visual indicating device for indicating the ability of an odor absorbing article to absorb odor, which includes at least one zone of a visual indicating agent that changes color when exposed to the odor, said zone having a concentration of the visual indicating agent that changes color to indicate that the article is saturated and should be replaced.

17. A method for visually indicating when an article for controlling odor is saturated comprising the steps of:

introducing into or onto the article a visual indicating agent that is color sensitive to the odor, and

observing the change in color of the indicating agent when the article is saturated with the odor.

18. The use of a visual indicating agent on an article for controlling odor, which provides an indication of when the article is saturated with the odor.

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PGPUB-DOCUMENT-NUMBER: 20050124072
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050124072 A1

TITLE: Personal care products with visual indicator of vaginitis

PUBLICATION-DATE: June 9, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Boga, RameshBabu	Roswell	GA	US
MacDonald, John Gavin	Decatur	GA	US

US-CL-CURRENT: 436/111

CLAIMS:

What is claimed is:

1. A personal care product comprising an indicator having at least one deposit of an amine sensitive dye, placed in said product such that said dye deposit is visible to an unaided eye.
2. The personal care product of claim 1 wherein said dye is present in an amount of between about 0.0001 and 20 weight percent on a dry basis.
3. The personal care product of claim 1 wherein said dye is selected from the group consisting of chemicals of the general formula (I) or (II) 8where, R, R' and R" may each independently be a substituted aryl group, a naphthyl group, heteroaryl groups and hydrogen.
4. The personal care product of claim 1 wherein said dye is selected from the group consisting of chemicals of the general formula (I) or (II) 9where, 10
5. The personal care product of claim 1 wherein said dye is selected from the group consisting of pararosaniline base (PAB), alpha-naphthol-benzein (ANB), and naphthochrome green (NCG) and mixtures thereof.
6. The personal care product of claim 1 wherein said indicator is selected from the group consisting of cellulose, woven or nonwoven fabric, cotton, silk, rayon, glass fiber, films, silica gels and latex particles.
7. The personal care product of claim 6 wherein said indicator is between about 0.25 and 3 centimeters in width and about 8 to 25 cm in length.
8. The personal care product of claim 6 wherein said indicator is between about 1 to 2 cm in width and about 10 to 15 cm in length.
9. The personal care product of claim 1 wherein said personal care product is selected from the group consisting of and feminine hygiene pads and absorbent underpants.

10. A feminine hygiene pad comprising a liquid impervious baffle, a liquid pervious body side liner and having a target area, and an indicator having two ends and having at least one dried, solution applied deposit of an amine sensitive dye near an end, and wherein said indicator extends from immediately below said liner in said target area to immediately above said baffle.
11. The feminine hygiene pad of claim 10 wherein said amine sensitive dye is selected from the group consisting of pararosaniline base (PAB), alpha-naphthol-benzein (ANB), and naphthochrome green (NCG) and mixtures thereof and is placed in sequential dots near at least one end of said indicator.
12. The pad of claim 10 wherein said indicator is between about 1 to 2 cm in width and about 10 to 15 cm in length.
13. The pad of claim 10 wherein only one end of said indicator is placed adjacent said baffle.
14. The pad of claim 10 wherein both ends of said indicator are placed adjacent said baffle.
15. The personal care product of claim 1 wherein said personal care product is selected from the group consisting of and feminine tampons, swabs, removable patches, absorbent underpants.
16. A method of providing a system for visually indicating the presence of amines that are characteristic of vaginitis, the method comprising: providing the feminine hygiene pad of claim 10, providing instructions to enable a user to properly place the pad, providing instructions to enable a user to visually examine the indicator at an appropriate time providing instructions to enable a user to visually interpret changes in the indicator; whereby a user is enabled to utilize the system to visually indicate the presence of amines that are characteristic of vaginitis.

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Boga, RameshBabu	Roswell	GA	US
MacDonald, John Gavin	Decatur	GA	US

Same inventor

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
Kimberly-Clark Worldwide, Inc.				

Same assignee

APPL-NO: 10/961676 [PALM]
DATE FILED: October 8, 2004

RELATED-US-APPL-DATA:

Application 10/961676 is a continuation-in-part of US application 10/729811, filed December 5, 2003, ABANDONED

INT-CL-PUBLISHED: [07] G01 N 33/00

US-CL-PUBLISHED: 436/111

US-CL-CURRENT: 436/111

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

There is provided a personal care product having a body side liner, a baffle and an indicator strip with two ends. The indicator has an amine sensitive dye near at least one end. The indicator extends from the target area just below the liner to just above the baffle such that the dye deposit is visible to an unaided eye. The dye changes color in the presence of amines which are characteristic of infection, thus alerting the user to the possibility of infection. Such an indicator placed in a feminine hygiene pad, for example, may be useful in the diagnosis of vaginitis.

[0001] This application is a Continuation-In-Part of U.S. patent application Ser. No. 10/729,811 filed Dec. 5, 2003, commonly assigned, and claims priority from that case.

PGPUB-DOCUMENT-NUMBER: 20060003336
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TITLE: One-step enzymatic and amine detection technique

PUBLICATION-DATE: January 5, 2006

INVENTOR-INFORMATION:

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Song; Xuedong	Roswell	GA	US
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Chidebelu-Eze; Chibueze Obi	Atlanta	GA	US

US-CL-CURRENT: 435/6; 435/23, 435/7.92

CLAIMS:

1. A diagnostic kit for detecting an amine, enzyme, or an enzyme inhibitor within a test sample, the kit comprising: a plurality of reactive complexes that each comprises a substrate joined to a reporter and a separation species, said substrate being cleavable by an enzyme to release said reporter; and a chromatographic medium that defines a first enzyme detection zone within which an enzyme detection signal is capable of being generated, wherein the presence or quantity of an enzyme, or an inhibitor thereof, is determinable from said enzyme detection signal, said chromatographic medium further, defining an amine detection zone within which is contained a chemichromic dye, said chemichromic dye being capable of undergoing a color change in the presence of an amine, wherein the presence or quantity of an amine is determinable from said color change.
2. A diagnostic test kit as defined in claim 1, wherein the enzyme is a protease or peptidase.
3. A diagnostic test kit as defined in claim 1, wherein said substrate is a protein, glycoprotein, peptide, nucleic acid, carbohydrate, lipid, ester, or derivative thereof.
4. A diagnostic test kit as defined in claim 1, wherein said substrate is casein, albumin, hemoglobin, myoglobin, keratin, gelatin, insulin, proteoglycan, fibronectin, laminin, collagen, elastin, or a derivative thereof.
5. A diagnostic test kit as defined in claim 1, wherein said reporter comprises a detectable substance that is capable of directly generating said enzyme detection signal.
6. A diagnostic test kit as defined in claim 1, wherein said reporter comprises a specific binding member.
7. A diagnostic test kit as defined in claim 6, further comprising probes conjugated with a specific binding member, said probes comprising a detectable substance that is capable of directly generating said enzyme detection signal.
8. A diagnostic test kit as defined in claim 1, wherein said separation species is a specific binding

member.

9. A diagnostic test kit as defined in claim 8, wherein a receptive material is immobilized within said first enzyme detection zone that has an affinity for said specific binding member.

10. A diagnostic test kit as defined in claim 1, wherein said separation species is a magnetic particle.

11. A diagnostic test kit as defined in claim 10, further comprising a magnetic device positioned adjacent to said chromatographic medium to immobilize said magnetic particle within a separation zone.

12. A diagnostic test kit as defined in claim 1, wherein said chromatographic medium further comprises a second enzyme detection zone within which a second enzyme detection signal is capable of being generated.

13. A diagnostic test kit as defined in claim 12, wherein a second receptive material is immobilized within said second detection zone that is capable of binding to said reporter or complexes thereof to generate said second enzyme detection signal.

14. A diagnostic test kit as defined in claim 12, wherein a second receptive material is immobilized within said second detection zone that is capable of binding to probes or complexes thereof to generate said second enzyme detection signal.

15. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is an arylmethane.

16. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is a triarylmethane having the following general structure: wherein R, R', and R" are independently selected from substituted and unsubstituted aryl groups.

17. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is a diarylmethane.

18. A diagnostic test kit as defined in claim 1, wherein said amine detection zone is positioned downstream from said first enzyme detection zone.

19. A diagnostic kit for detecting an amine or a hydrolytic enzyme within a test sample, the kit comprising: a plurality of reactive complexes that each comprises a substrate joined to a reporter and a specific binding member, said substrate being cleavable by a hydrolytic enzyme to release said reporter; and a chromatographic medium that defines a first enzyme detection zone within which an enzyme detection signal is capable of being generated, wherein the presence or quantity of a hydrolytic enzyme is determinable from said enzyme detection signal, said chromatographic medium further defining an amine detection zone positioned downstream from said first enzyme detection zone, wherein a chemichromic dye is contained within said amine detection zone, said chemichromic dye being capable of undergoing a color change in the presence of an amine, wherein the presence or quantity of an amine is determinable from said color change.

20. A diagnostic test kit as defined in claim 19, wherein said reporter comprises a detectable substance that is capable of directly generating said enzyme detection signal.

21. A diagnostic test kit as defined in claim 19, wherein said reporter comprises a specific binding member.

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22. A diagnostic test kit as defined in claim 21, further comprising probes conjugated with a specific binding member, said probes comprising a detectable substance that is capable of directly generating said enzyme detection signal.
23. A diagnostic test kit as defined in claim 19, wherein said chromatographic medium further comprises a second enzyme detection zone within which a second enzyme detection signal is capable of being generated.
24. A diagnostic test kit as defined in claim 23, wherein said second detection zone is capable of capturing said reporter or complexes thereof to generate said second enzyme detection signal.
25. A diagnostic test kit as defined in claim 19, wherein said chemichromic dye is a triarylmethane having the following general structure: wherein R, R', and R" are independently selected from substituted and unsubstituted aryl groups.
26. A diagnostic test kit as defined in claim 19, wherein said chemichromic dye is a diarylmethane.
27. A method for detecting an amine, enzyme, or enzyme inhibitor within a test sample, the method comprising: i) contacting the test sample with a chromatographic medium, said chromatographic medium defining an enzyme detection zone and an amine detection zone, wherein an enzyme detection signal is capable of being generated within said enzyme detection zone and an amine detection signal is capable of being generated within said amine detection zone; ii) determining the presence or quantity of an enzyme or enzyme inhibitor from said enzyme detection signal; and iii) determining the presence or quantity of an amine from said amine detection signal.
28. A method as defined in claim 27, wherein the quantity of an enzyme within the test sample is inversely proportional to the intensity of said enzyme detection signal.
29. A method as defined in claim 27, wherein the quantity of an enzyme within the test sample is directly proportional to the intensity of said enzyme detection signal.
30. A method as defined in claim 27, wherein said chromatographic medium further comprises a second enzyme detection zone within which a second enzyme detection signal is capable of being generated.
31. A method as defined in claim 30, wherein the quantity of an enzyme within the test sample is directly proportional to the intensity of said second enzyme detection signal.
32. A method as defined in claim 27, further comprising selectively controlling the pH level of the test sample to optimize the activity of an enzyme.
33. A method as defined in claim 27, wherein the test sample is obtained from vaginal fluid.

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TITLE: One-step enzymatic and amine detection technique

PUBLICATION-DATE: January 5, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
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Boga; RameshBabu	Roswell	GA	US
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different invention entity

ASSIGNEE-INFORMATION:

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assignee

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DATE FILED: June 30, 2004

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IPCS	G01N33/573	20060101	G01N033/573
IPCS	G01N33/53	20060101	G01N033/53

INT-CL-CURRENT:

TYPE	IPC	DATE
CIPS	G01 N 33/53	20060101
CIPS	G01 N 33/573	20060101
CIPP	C12 Q 1/68	20060101

US-CL-PUBLISHED: 435/006; 435/007.92, 435/023

US-CL-CURRENT: 435/6; 435/23, 435/7.92

ABSTRACT:

A technique for detecting the presence or quantity of an enzyme (or enzyme inhibitor) and/or an amine within a test sample is provided. For example, in one embodiment, a diagnostic test kit is employed that utilizes reactive complexes that each includes a substrate joined (e.g., covalently bonded, physically adsorbed, etc.) to a reporter and a separation species. Upon contacting the reactive complexes, enzymes may cleave the substrate and release the reporter. Moreover, the test kit may also employ a chemichromic dye, i.e., a dye that exhibits a detectable color change upon chemical reaction with one or more functional groups, such as amino groups. The signal generated (directly or indirectly) by the reporter and chemichromic dye may then be used to indicate the presence or quantity of an enzyme (or

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approximately 10 min. after shifting the growth temperature from 28°C to 42°C with gene *E* under transcriptional control of the Lambda P_R/P_L-cI857 system. Several E-specific lysis plasmids with different resistance markers, origins of replication and gene *E* expression control have been published (Szostak et al., 1996). In a modified procedure of E-mediated lysis (alternative E-lysis) high concentrations of MgSO₄ are used to inhibit transmembrane tunnel formation. Before induction of gene *E* expression 0.2 M MgSO₄ is added to the growth medium. Gene *E* expression is induced 30 min. later and is allowed to proceed for another 30 min. before cells are harvested by centrifugation. Resuspension of the cell pellet, either in water or low ionic strength buffers, causes immediate lysis of the cells (Figure 1). Electron micrographs showed that Mg-lysis induces larger holes in cell envelopes either in the middle of the cells or at the periseptal anuli (Figure 1).

E-mediated lysis from plasmids with *E. coli*-related origins of replication has been achieved in various *Escherichia coli* strains, *Salmonella typhimurium*, *Salmonella enteritidis*, *Klebsiella pneumoniae*, *Bordetella bronchiseptica*, *Helicobacter pylori*, and *Vibrio cholerae*. For *Actinobacillus pleuropneumoniae*, *Haemophilus influenzae*, *Pasteurella haemolytica* and *Pasteurella multocida*, new shuttle vectors with additional origins of replication were constructed.

Recombinant Bacterial Ghosts

For the production of combination vaccines against bacterial and viral pathogens or to use bacterial ghosts as carrier systems for other antigens, a membrane targeting system was developed for the attachment of foreign protein entities to the inner side of the cytoplasmic membrane (Lubitz and Szostak, 1991; Szostak and Lubitz, 1991). By cloning the foreign DNA sequences into the membrane targeting vector pMTV5, any antigen gene can be

expressed from the inducible lac promoter as a hybrid protein with N-, C- or N-/C-terminal membrane anchors directing and attaching the fusion protein to the envelope complex of the bacteria prior to E-mediated lysis. Humoral and cellular immune responses to the carrier ghost and target antigens which are embedded into the highly immune-stimulatory environment of the cell envelope have been determined (Szostak et al., 1996). The adjuvant components of the envelope comprise LPS, peptidoglycan, lipids and all other attractants of the envelope complex contributing to effective uptake by primary antigen presenting cells.

Recombinant S-Layer Proteins in Combination with (Recombinant) Ghosts as Candidate Vaccines

The surface layer (S-layer) gene *sbsA* of *Bacillus stearothermophilus* has recently been sequenced (Kuen et al., 1994) and heterologous expression of the cloned *sbsA* gene in *E. coli* has been achieved (Kuen et al., 1995). As shown by ultrathin sectioning of whole cells and immunogold labelling using SbsA-specific antibodies, expression of *sbsA* in *E. coli* led to accumulation of sheet-like self-assembling SbsA proteins in the cytoplasm (Kuen et al., 1995). Site-directed mutagenesis of *sbsA* and structural/functional analysis of S-layer domains essential for intra- and/or intermolecular interactions revealed flexible surface loops which accept foreign sequences of up to 600 amino acids. The recombinant S-layer proteins (rS-layer) showed self-assembly structures identical to the wild-type SbsA (Figure 2 e,f). Such flexible recombinant surface loops of SbsA are desirable in vaccinology as carriers of foreign epitopes (Figure 2). With rSbsA proteins the immune response against specific proteins of recombinant bacterial ghosts can be boosted to enhance the immune response against corresponding bacterial or viral target antigens (Figure 2 a-c). In addition,

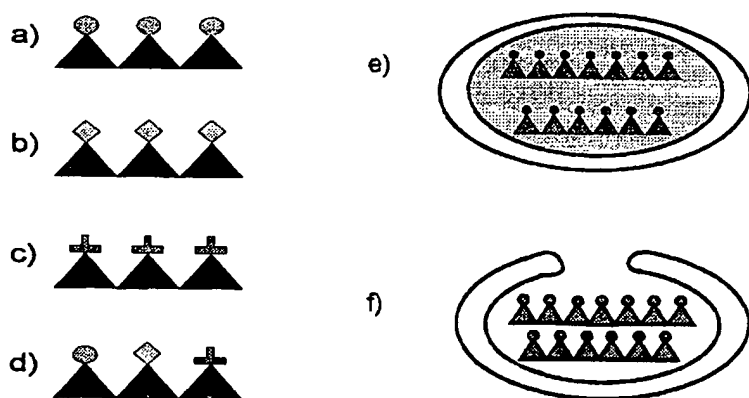


Fig. 2: Recombinant SbsA proteins as carriers of target antigens. a-c) Different rSbsA constructs carrying different target antigens in flexible surface loops. d) Three different rSbsA proteins have been dissociated and recrystallized into a multivaccine rSbsA structure. e) The expression of rSbsA in *E. coli* leads to the formation of sheet-like S-layer structures in the cytoplasm of the cells. f) Bacterial ghost carrying sheet-like rSbsA proteins with target epitopes in the inner space of the cell envelope.

multivaccine components can be derived by mixing together multiple, different r-SbsA subunits, each carrying relevant immunodeterminants of pathogens (Figure 2 d).

Induction of Immune Responses to Bacterial Ghosts in Experimental Animals

In order to determine the humoral immune response to bacterial ghosts, different experimental animals including mice, rabbits and pigs were used. They were immunized either by the intraperitoneal, subcutaneous or aerogenic route with or without booster immunizations. Serum samples were analysed by ELISA using nonkilled whole cells, heat or X-ray inactivated cells, ghosts or specific target proteins as coating antigens. Analysis of the immune responses of such ghosts in different animal models indicates that ghosts induce humoral and cellular immune responses against cell envelope constituents including protective immunity against challenge infections (Hensel et al., 1995, 1996; Szostak et al., 1996).

Endotoxicity of Bacterial Ghosts does not Limit their Use as Candidate Vaccines

The endotoxin content of the Gram-negative cell wall has been suggested as a potential problem for non-living vaccines. Bacterial ghosts prepared from *Escherichia coli* O26:B6 and *Salmonella typhimurium* C5 which induced dose-dependent antibody responses against bacterial cells or their corresponding LPS in doses from 25 to 250 ng kg⁻¹ when administered intravenously to rabbits in a standard immunization protocol, did not induce significant fever responses as determined by test methods recommended by the US-pharmacopoeia (Mader et al., 1996).

Bacterial Ghosts as Adjuvants

The ability to induce an immune response depends not only on the molecular properties of the antigen or on the immunogenic susceptibility of the host but also on the antigen formulation. Adjuvants like tapioca, Alum, Freund's adjuvants, LPS and other cell wall

constituents as well as some others have been used to specifically the immune response. Although it is not each of the adjuvants a immune response, it is the deposition of the antigen is one of the major properties. A second important role of macrophages and anti resulting in the release of immune response. Bacterial up of compounds some known immune stimulant and peptidoglycan. The ghosts used as carriers should enhance the immune target antigens.

When compared to the HIV-1 RT formulated with CFA, following subcutaneous evoked an enhanced immune response of the same magnitude for all. With the intraperitoneal ghosts induced an IgG response with CFA or with Alum.

It remains to be elucidated of the target antigens packaging of antigens in the envelopes results in a response against the foreign

Acknowledgements

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constituents as well as microspheres and liposomes have been used to potentiate nonspecifically the immune response to a target antigen. Although it is not fully understood how each of the adjuvants act to enhance an immune response, it is believed that prolonged deposition of the antigen at the injection site is one of the major properties of adjuvants. A second important role is the activation of macrophages and antigen presenting cells resulting in the release of modulators of the immune response. Bacterial ghosts are built up of compounds some of which are well-known immune stimulants like LPS or lipid A and peptidoglycan. Thus, ghosts *per se* or ghosts used as carriers of foreign proteins should enhance the immune response against target antigens.

When compared to the immunogenicity of HIV-1 RT formulated with ghosts, Alum or CFA, following subcutaneous application, RT evoked an enhanced immune response of the same magnitude for all three formulations. With the intraperitoneal route, RT mixed with ghosts induced an IgG response higher than with CFA or with Alum (Szostak et al., 1993).

It remains to be elucidated which formulation of the target antigens packed into the ghost envelope structures either as membrane anchored proteins or as paracrystalline recombinant S-layer proteins or whether loose packaging of antigens into the inner space of the envelopes results in enhanced immune response against the foreign antigens.

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- Szostak, M., Auer, T. & Lubitz, W.** (1993) Immune response against recombinant bacterial ghosts carrying HIV-1 reverse transcriptase. In: *Vaccines 93: Modern Approaches to New Vaccines Including Prevention of AIDS* (Chanock, R. M. et al., Eds.), Cold Spring Harbor Laboratory Press, New York, p.p. 419-425.
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Bacterial Antigen D
Antigens for MHC
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Summary

Using an in vitro model system, we have shown that antigen-presenting cells that influence the presentation of a peptide epitope, which binds the MHC-II (MHC-II) and class I (MHC-I) fusion protein in the endosome, enhance the efficiency of antigen processing of S. typhimurium presented on I-A^k more efficiently than on I-E^k. This effect was from a rough LPS strain of S. typhimurium enhanced phagocytosis of S. typhimurium strains with greater roughness, while Salmonella constitutively rough strains were less efficiently than wild type strains. E. coli or S. typhimurium rough strains investigated the role of post-phagocytosis of macrophages from TAP-1-deficient mice. MHC-I and lack significant differences in containing the 257-264 epitope of OVA. Peritoneal macrophages presented OVA epitope for recognition. This suggests that the protein has an independent processing for MHC-I and MHC-II-derived dendritic cells. The results show that peptide presentation on MHC-I and MHC-II in dendritic cells are required for antigen presentation. be potential antigen presentation.

Key-Words: MHC-I, MHC-II

Antigen Processing and Pres

Antigen processing and process whereby proteins peptides that are presented are eukaryotic cells for recognition

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Bacterial Ghosts as Multifunctional Vaccine Particles

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Summary

Expression of cloned PhiX174 gene E in Gram-negative bacteria results in lysis of the bacteria by formation of an E-specific transmembrane tunnel structure built through the cell envelope complex. Bacterial ghosts have been produced from a variety of bacteria including Escherichia coli, Salmonella typhimurium, Salmonella enteritidis, Vibrio cholerae, Klebsiella pneumoniae, Actinobacillus pleuropneumoniae, Haemophilus influenzae, Pasteurella haemolytica, Pasteurella multocida, and Helicobacter pylori. Such ghosts are used as non-living candidate vaccines and represent an alternative to heat or chemically inactivated bacteria. In recombinant ghosts, foreign proteins can be inserted into the inner membrane prior to E-mediated lysis via specific N-, or C-, or N- and C-terminal anchor sequences. The export of proteins into the periplasmic space or the expression of recombinant S-layer proteins vastly extends the capacity of ghosts or recombinant ghosts as carriers of foreign epitopes or proteins. Oral, aerogenic or parenteral applications of (recombinant) ghosts in experimental animals induced specific humoral and cellular immune responses against bacterial and target components including protective mucosal immunity. The most relevant advantage of ghosts and recombinant bacterial ghosts as immunogens is that no inactivation procedures that denature relevant immunogenic determinants are employed in the production of ghosts used as vaccines or as carriers of relevant antigens. The inserted target antigens into the inner membrane or into S-layer proteins are not limited in size.

Key-Words: Bacterial ghost, multi-vaccines, genetic inactivation, carrier system, adjuvants.

Introduction

Vaccination with killed pathogenic microorganisms enables the immune system to come into a riskless contact with an otherwise life-threatening pathogen. The use of killed pathogens as substitutes for the living infectious agents has been widely used as a principle for vaccine development. Non-living vaccines can easily be produced by chemical or physical activation of pathogenic bacteria. In comparison with subunit vaccines, non-living whole-cell vaccines have the advantage of presenting a complex array of antigenic determinants to the immune system. However, common methods of inactivating infectious agents

like heat-killing, irradiation or chemical treatment often result in reducing or altering the vaccine's antigenic character and could be responsible for the loss of relevant immunogenic epitopes (Miyamae, 1986; Holt et al., 1990; Melamed et al., 1991; Nencioni et al., 1991; Ferguson et al., 1993).

Genetic inactivation of pathogenic bacteria by the controlled expression of cloned bacteriophage PhiX174 lysis gene E offers a promising new approach in non-living vaccine technology. Expression of plasmid-encoded gene E leads to the formation of a transmembrane tunnel structure through the cell envelope of Gram-negative bacteria. The resulting

enzyme inhibitor) and amine, respectively, within the test sample.

DOCUMENT-IDENTIFIER: US 20060003336 A1

TITLE: One-step enzymatic and amine detection technique

Description of Disclosure:

[0052] Of course, any other suitable technique for capturing and detection the released reporters may also be used. For example, in some embodiments, non-biological receptive materials may be immobilized within the second enzyme detection zone 35 for capturing released reporters. Such non-biological receptive materials may be particularly useful in capturing, for example, released reporters that contain labeled particles. For instance, in one embodiment, the receptive material is a polyelectrolyte. Polyelectrolytes may have a net positive or negative charge, as well as a net charge that is generally neutral. Some suitable examples of polyelectrolytes having a net positive charge include, but are not limited to, polylysine (commercially available from Sigma-Aldrich Chemical Co., Inc. of St. Louis, Mo.), polyethylenimine; epichlorohydrin-functionalized polyamines and/or polyamidoamines, such as poly(dimethylamine-co-epichlorohydrin); polydiallyldimethyl-ammonium chloride; cationic cellulose derivatives, such as cellulose copolymers or cellulose derivatives grafted with a quaternary ammonium water-soluble monomer; and so forth. In one particular embodiment, CelQuat.RTM. SC-230M or H-100 (available from National Starch & Chemical, Inc.), which are cellulosic derivatives containing a quaternary ammonium water-soluble monomer, may be utilized. Moreover, some suitable examples of polyelectrolytes having a net negative charge include, but are not limited to, polyacrylic acids, such as poly(ethylene-co-methacrylic acid, sodium salt), and so forth. It should also be understood that other polyelectrolytes may also be utilized in the present invention, such as amphiphilic polyelectrolytes (i.e., having polar and non-polar portions). For instance, some examples of suitable amphiphilic polyelectrolytes include, but are not limited to, poly(styryl-b-N-methyl 2-vinyl pyridinium iodide) and poly(styryl-b-acrylic acid), both of which are available from Polymer Source, Inc. of Dorval, Canada. Further examples of polyelectrolytes are described in more detail in U.S. Patent App. Publication No. 2003/0124739 to Song, et al., which is incorporated herein in its entirety by reference thereto for all purposes.

Description of Disclosure:

[0069] Triarylmethane dyes, for example, may have the following general structure: wherein R, R', and R" are independently selected from substituted and unsubstituted aryl groups, such as phenyl, naphthyl, anthracenyl, etc. The aryl groups may, for example, be substituted with functional groups, such as amino, hydroxyl, carbonyl, carboxyl, sulfonic, alkyl, and/or other known functional groups. When contacted with the dye, the amino group of the amine (e.g., ammonia, diamines, and/or tertiary amines) reacts with the central carbon atom of the dye. The addition of the amino group causes the dye to undergo a change in color. An example of the resulting structure is set forth below:

Description of Disclosure:

[0071] In some cases, triarylmethane dyes may be formed by converting a leuco base to a colorless carbinol and then treating the carbinol with an acid to oxidize the carbinol and form the dye. Thus, for example, pararosanilin may be derived by reacting the carbinol form of pararosanilin ("pararosaniline base") with an acid, such as, but not limited to, sulfonic acids, phosphoric acids, hydrochloric acid, and so forth. The carbinol form of pararosanilin is set forth below.

Description of Disclosure:

[0074] As indicated above, diarylmethanes may also be used in the present invention. One example of such a diarylmethane is 4,4'-bis (dimethylamino) benzhydrol (also known as "Michler's hydrol"), which has the following structure:

Description of Disclosure:

[0075] Still other examples include analogs of Michler's hydrol, such as Michler's hydrol leucobenzotriazole, Michler's hydrol leucomorpholine, Michier's hydrol leucobenzenesulfonamide, and so forth, as well as other diarylmethanes, such as malachite green leuco, malachite green carbinol, sodium 2,6-dichloroindopheno-late, rhodamine lactam, crystal violet lactone, and crystal violet leuco.

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Evaluation of *p*-Naphtholbenzein- β -D-Galactoside as a Substrate for Bacterial β -Galactosidase

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We describe the synthesis of a new substrate for the detection of β -galactosidase and evaluate its performance in comparison with 5-bromo-4-chloro-3-indolyl- β -D-galactopyranoside (X-Gal) and cyclohexenoescluletin- β -D-galactoside (CHE-Gal). Of 206 *Enterobacteriaceae* strains able to hydrolyze X-Gal, 194 (94.2%) hydrolyzed CHE-Gal and 192 (93.2%) hydrolyzed *p*-naphtholbenzein- β -D-galactoside (PNB-Gal). We conclude that PNB-Gal is an effective substrate for the detection of β -galactosidase.

The enzyme β -galactosidase has long been regarded as an important taxonomic marker in microbial identification, particularly among gram-negative species. The long-established *ortho*-nitrophenyl- β -D-galactopyranoside test relies on the hydrolysis of *ortho*-nitrophenyl- β -D-galactoside by β -galactosidase, releasing yellow *ortho*-nitrophenol (5). Fluorogenic galactosides such as those based on fluorescein, resorufin, and 4-methylumbelliferone are also well established (1, 8). When agar-based methods are used, chromogenic substrates that yield insoluble products are desired so that the aglycone released by hydrolysis does not diffuse widely (3, 6). Indoxyl galactosides such as indoxyl- β -galactoside and its halogenated derivatives, including 5-bromo-4-chloro-3-indolyl- β -D-galactopyranoside (X-Gal), have advantages when used in solid media, as the aglycone released is oxidized rapidly by air to produce an insoluble colored product which is restricted to the colony mass (4). Although these substrates are very effective when used aerobically, their synthesis is not straightforward. Although many substrates for β -galactosidase have been described, there are few alternatives to indoxyl-based substrates suitable for inclusion in agar-based media. One alternative is to use a galactoside derivative of cyclohexenoescluletin, a core molecule which forms an insoluble black chelate when released by hydrolysis (3). Such substrates require the inclusion of iron in the medium, which can be a disadvantage as deaminase activity may also generate colored products in the presence of peptone and iron (2, 7).

We describe the synthesis of a new chromogenic substrate for the detection of β -galactosidase, *p*-naphtholbenzein- β -D-galactopyranoside (PNB-Gal) (Fig. 1). The *p*-naphtholbenzein released by hydrolysis remains localized on bacterial colonies that appear pink. The effectiveness of this substrate was evaluated in direct comparison to cyclohexenoescluletin- β -D-galactoside (CHE-Gal) and X-Gal for the detection of β -galactosidase within the *Enterobacteriaceae* and other gram-negative species.

p-Naphtholbenzein was obtained from Acros Organics, Geel, Belgium. CHE-Gal was synthesized by a method described previously (3). All other chemicals and materials were obtained from the Sigma-Aldrich Chemical Company Ltd., Poole, United Kingdom. The synthesis of PNB-Gal was as

follows. Five millimoles of *p*-naphtholbenzein (1.87 g) was dissolved in 20 ml of acetone with vigorous stirring. A 5-ml solution containing 1.4 mol of potassium hydroxide/liter was added to this followed by an additional 10 ml of acetone. Approximately 5 ml of water was then added dropwise to generate a homogeneous deep-blue solution. Ten millimoles of α acetobromogalactose (4.1 g) was dissolved in 10 ml of acetone and added to this solution. In order to maintain the pH above 11, 2 ml of a 20-mol/liter potassium hydroxide solution was added after 30 min of stirring and again after 90 min. After 3.5 h, a further 2 ml of alkali was added followed by an additional 5 ml of α acetobromogalactose in acetone. After 4.5 h, another 2 ml of alkali was added and the solution was left, with stirring, overnight.

The acetone was removed under reduced pressure, and the residual solution was poured into 300 ml of a 0.06-mol/liter sodium carbonate solution at 0°C with good stirring. The brown precipitate was separated by vacuum filtration, washed with water, and air dried. This solid was dissolved in 100 ml of dichloromethane and washed thoroughly with 0.5 mol of potassium hydroxide/liter at 0°C to remove most of the free *p*-naphtholbenzein. Residual *p*-naphtholbenzein was removed by stirring with Dowex Marathon resin in 100 ml of water at pH 11.0 for 2 to 3 h. The purification was followed by thin-layer chromatography using ethyl acetate-toluene (3:1) as the solvent, with subsequent transient exposure of the chromatogram to ammonia.

The deep-yellow solution was dried overnight using anhydrous magnesium sulfate and was evaporated, reconstituted with methanol, and evaporated to produce a mousse. The mousse was directly dissolved in 50 ml of methanol and deprotected over 5 h using a 20-ml solution containing 0.4 mol of sodium methoxide/liter of methanol. The methanolic solution was adjusted to pH 6.5 using ion-exchange resin (120[H⁺]) and was separated by decantation and the solvent removed under reduced pressure. The glycoside formed a brownish yellow powder. This was removed, yielding 1.5 g of PNB-Gal.

All galactosides used in this study were added to the media prior to autoclaving, which is normal practice in our laboratory. PNB-Gal agar was prepared as follows: 41 g of Columbia agar was added to 1 liter of distilled water, along with 100 mg of PNB-Gal. A 30-mg sample of the gratuitous inducer isopropyl- β -D-thiogalactopyranoside (IPTG) was also included, to aid the induction of β -galactosidase. The agar was sterilized by autoclaving for 10 min at 116°C. The medium was then allowed to cool to 55°C before being poured into 20-ml volumes. Both

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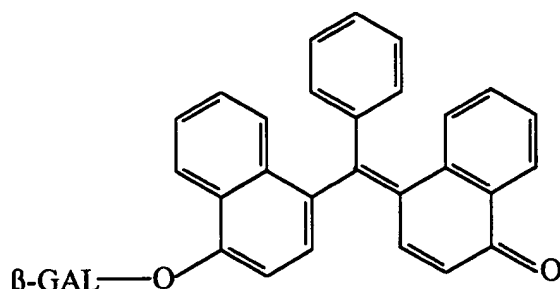


FIG. 1. Structure of PNB-Gal.

CHE-Gal agar and X-Gal agar were prepared in identical fashion, except that 300 mg of CHE-Gal and 80 mg of X-Gal were substituted for PNB-Gal, respectively. Ferric ammonium citrate (500 mg/liter) was also included in CHE-Gal agar to allow formation of the metal chelate. A duplicate batch of X-Gal agar was prepared in which the X-Gal was added after autoclaving once the agar had cooled to 50°C. Each chromogenic medium was also prepared with IPTG excluded to assess the performance of each substrate in the absence of an enzyme inducer. In order to investigate the sensitivity of PNB-Gal, two more agars were prepared with a reduced substrate concentra-

tion (50 and 20 mg/liter); both were prepared as described above with IPTG included.

Strains (397) of a range of species, including 333 *Enterobacteriaceae* collected from a wide range of clinical and environmental samples, were identified using the API 20 E system (bioMérieux). These strains were cultivated on Columbia agar at 37°C for 24 h. Each strain was then inoculated into physiological saline to produce an inoculum of approximately 10^8 organisms per ml (equivalent to a McFarland standard of 0.5). Using a multipoint inoculator (Denley), 1 μ l of each suspension was then inoculated onto all three of the test media and Columbia agar as a growth control. Twenty strains were inoculated per plate.

All plates were incubated at 37°C for exactly 18 h. After incubation, PNB-Gal plates were examined for the presence of pink colonies, CHE-Gal plates for the presence of black colonies, and X-Gal plates for the presence of blue colonies; Columbia agar plates were examined for growth as well.

From the results shown in Table 1 it can be concluded that PNB-Gal showed good correlation with both X-Gal and CHE-Gal. Of 206 *Enterobacteriaceae* strains able to hydrolyze X-Gal, 194 (94.2%) hydrolyzed CHE-Gal and 192 (93.2%) hydrolyzed PNB-Gal. None of the strains which failed to hydrolyze X-Gal produced any coloration with the other substrates; i.e., there were no false-positive results. The addition of X-Gal prior to autoclaving had no detectable impact on its performance. The

TABLE 1. Hydrolysis of different β -galactosidase substrates by strains of *Enterobacteriaceae* and related species

Gram-negative species	No. of strains	% Positive with substrate					
		PNB-Gal with IPTG	PNB-Gal	X-Gal with IPTG	X-Gal	CHE-Gal with IPTG	CHE-Gal
<i>Acinetobacter</i> spp.	53	0	0	0	0	0	0
<i>Aeromonas caviae</i>	7	86	86	86	86	86	86
<i>Aeromonas hydrophila</i>	3	100	100	100	100	100	100
<i>Citrobacter diversus</i>	9	89	78	89	89	89	67
<i>Citrobacter freundii</i>	16	100	81	100	100	100	100
<i>Enterobacter aerogenes</i>	9	100	67	100	100	100	100
<i>Enterobacter agglomerans</i>	1	100	100	100	100	100	100
<i>Enterobacter cloacae</i>	21	100	95	100	100	100	95
<i>Escherichia coli</i>	71	83	82	83	83	83	82
<i>Escherichia hermannii</i>	1	100	0	100	100	100	100
<i>Hafnia alvei</i>	10	70	70	90	90	80	80
<i>Klebsiella oxytoca</i>	13	100	100	100	100	100	100
<i>Klebsiella ozaenae</i>	3	33	33	33	33	33	33
<i>Klebsiella pneumoniae</i>	19	100	89	100	89	100	100
<i>Morganella morganii</i>	12	0	0	0	0	0	0
<i>Proteus mirabilis</i>	16	0	0	0	0	0	0
<i>Proteus penneri</i>	1	0	0	0	0	0	0
<i>Proteus vulgaris</i>	4	0	0	0	0	0	0
<i>Providencia alcalifaciens</i>	3	0	0	0	0	0	0
<i>Providencia rettgeri</i>	3	0	0	0	0	0	0
<i>Providencia stuartii</i>	10	0	0	0	0	0	0
<i>Salmonella</i> spp.	64	0	0	0	0	0	0
<i>Serratia odorifera</i>	1	100	100	100	100	100	100
<i>Serratia liquefaciens</i>	6	83	83	100	100	83	83
<i>Serratia marcescens</i>	8	75	75	100	88	100	100
<i>Shigella boydii</i>	1	0	0	0	0	0	0
<i>Shigella dysenteriae</i>	2	0	0	0	0	0	0
<i>Shigella flexneri</i>	2	0	0	0	0	0	0
<i>Shigella sonnei</i>	10	100	100	100	100	100	100
<i>Vibrio cholerae</i>	1	100	100	100	100	0	0
<i>Yersinia enterocolitica</i>	14	36	36	100	100	36	36
<i>Yersinia pseudotuberculosis</i>	3	0	0	0	0	0	0
Total no. of strains	397						
Overall % positive		48.3	45.4	51.9	51.1	48.8	47.9

performance of X-Gal was least affected when IPTG was excluded, when it still detected 98.5% of β -galactosidase producers compared with 92.2% by CHE-Gal and 87.4% by PNB-Gal. Overall, there were only a small number of discrepancies between these three substrates; however, there was substantial variation in the ability of the substrates to detect β -galactosidase produced by *Yersinia enterocolitica*. For example, X-Gal detected β -galactosidase in all strains of *Y. enterocolitica*, whereas only 5 of 14 *Y. enterocolitica* strains (36%) were detected as weakly positive with both CHE-Gal and PNB-Gal.

In all cases, strains which hydrolyzed PNB-Gal produced a clearly visible pink precipitate that remained highly restricted to the bacterial colony. Reducing the concentration of PNB-Gal resulted in a reduced sensitivity of the substrate. For example, when PNB-Gal was used at 50 mg/liter, 91.3% of positives were detected, and when it was tested at 20 mg/liter, 88.8% of positives were detected.

We have shown that PNB-Gal is able to detect β -galactosidase activity in strains of *Enterobacteriaceae* and that its performance stands good comparison with that of both X-Gal and CHE-Gal. The substrate is highly sensitive at low concentrations, and its performance is almost identical to that of CHE-Gal when used at one-third the concentration. Even at 20 mg/liter, if strains of *Y. enterocolitica* are excluded, PNB-Gal detected 94.3% of all β -galactosidase producers. This is one quarter of the concentration used for X-Gal and 1/15 of the optimal concentration of CHE-Gal. The synthesis of PNB-Gal is very straightforward and cost-effective. This is because, unlike CHE-Gal and X-Gal, the core molecule required for derivatization is available commercially and is inexpensive, thus simplifying the synthetic process. This factor, combined with the high sensitivity of the substrate, makes the use of PNB-Gal highly economical.

A further advantage of PNB-Gal is that cofactors are not required for generation of the colored product, as the core molecule is naturally colored and relatively insoluble. This offers a greater flexibility when using such substrates in chromogenic media, whereas X-Gal and CHE-Gal require oxygen and metal ions, respectively, for the generation of color.

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<input type="checkbox"/>	L9	pararosaniline	623
<input type="checkbox"/>	L10	L9 and ammonia	274
<input type="checkbox"/>	L11	L10 and (bdmb or michler\$ or \$benzhydrol)	19
<input type="checkbox"/>	L12	l1 and (apparatus or device or detect\$.ti.	3316
<input type="checkbox"/>	L13	l1 and (apparatus or device).ti.	2964
<input type="checkbox"/>	L14	L13 and (visual or color or dye or sensitive or change or green or blue or purple or violet or yellow or red).ti,ab.	201
<input type="checkbox"/>	L15	l1 and helicobacter	34
<input type="checkbox"/>	L16	6495102.pn.	2

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- ☐ 2. [20050084977](#). 16 Oct 03. 21 Apr 05. Method and device for detecting ammonia odors and helicobacter pylori urease infection. Boga, RameshBabu, et al. 436/113; G01N033/53 G01N033/00.
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- ☐ 9. [US20050084977A](#). Breath testing device for detecting the presence of ammonia odors and helicobacter pylori urease infection, comprises a visual indicating agent, which is color sensitive to ammonia. BOGA, R, et al. G01N033/00 G01N033/53.
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- ☐ 12. [WO2003041565A](#). Detecting Helicobacter pylori infection in a subject's expiration, by

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☐ 13. JP2002360294A. Confirming the effectiveness of a chemical agent against Helicobacter pylori, comprises adding a test drug to culture medium containing urea, cultivating Helicobacter pylori and measuring the conversation of urea into ammonia. C12Q001/04.

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- ☐ 85. US20030126868A. Separating and neutralizing apparatus for entrained ammonia, has in-line pump which pumps mixture of aqueous media, acid, and released ammonia from treatment tank and circulates mixture through closed system of recirculation piping. BERTRAND, M R, et al. F25B043/02 F25B043/04.
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- ☐ 89. [US 6544908B](#). Passivating interface in semiconductor device, involves disassociating ammonia to expose adjacent structure at interface with hydrogen species and forming encapsulant layer. GONZALEZ, F, et al. H01L021/26 H01L021/31.
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- ☐ 90. [DE 10205838C](#). Analysis apparatus for determining concentration of nitrite, nitrate, ammonia, ammonium ions and phosphate in fish-rearing tanks or clarification basins has single test tube automatically filled with sample and reactants. KUFNER, J, et al. G01N021/11 G01N021/25 G01N021/78.
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- ☐ 95. [US20020096236A](#). Preparation of azide-free gas generant composition, for pyrotechnic devices e.g. airbag inflators, comprises grinding nitroguanidine into amorphous crumb and then mixing with phase stabilized ammonium nitrate. ADAMS, J H, et al. C06B021/00 C06B031/32 C06D005/00 C06D005/06 D03D023/00 D03D043/00.
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- ☐ 96. [US 6406669B](#). Optical ammonia gas sensing apparatus, useful for quantitatively determining amount of ammonia in fluid, comprises transparent polyaniline film, spectrometer, optical fiber, charge coupled device detector, and computer. DUAN, Y, et al. G01N021/77.
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☐ 97. EP 1213331A. Recording liquid for inkjet recording apparatus, comprises coloring agent, water, polyol having preset water solubility at specific temperature, and amine oxide and/or quaternary ammonium compound. ARITA, H, et al. B41J002/01 B41M005/00 C09D011/00 G01D011/00.

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☐ 100. EP 1191005A. Gas-generating composition for air bag system of vehicle passenger-protecting apparatus, contains ammonium nitrate, organic binder and stabilizer consisting of preset nitrogen-containing compound. SERIZAWA, K, et al. B01J007/00 B60R021/20 B60R021/26 B60R022/46 C06B023/00 C06B031/28 C06B031/30 C06B045/10 C06D005/00 C06D005/06.

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CHANGE	2714031
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- ☐ 1. [20050084977](#). 16 Oct 03. 21 Apr 05. Method and device for detecting ammonia odors and helicobacter pylori urease infection. Boga, RameshBabu, et al. 436/113; G01N033/53 G01N033/00.
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Term	Documents
(4 AND 1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	8
(L4 AND L1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	8

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First Hit

L5: Entry 1 of 8

File: PGPB

Apr 21, 2005

PGPUB-DOCUMENT-NUMBER: 20050084977

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050084977 A1

TITLE: Method and device for detecting ammonia odors and helicobacter pylori urease infection

PUBLICATION-DATE: April 21, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Boga, RameshBabu	Roswell	GA	US
MacDonald, John Gavin	Decatur	GA	US

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
Kimberly-Clark Worldwide, Inc.				02

APPL-NO: 10/687327 [PALM]

DATE FILED: October 16, 2003

INT-CL-PUBLISHED: [07] G01 N 33/53, G01 N 33/00

US-CL-PUBLISHED: 436/113










US-CL-CURRENT: 436/113

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The invention provides a breath testing device which visually indicates the presence of ammonia in a patient's breath, in particular ammonia from helicobacter pylori urease infection. The breath testing device comprises a visual indicating agent which changes color in response to ammonia odors, such as 4,4'-bis (dimethylamino)-benzhydrol (Michler's hydrol or BDMB), pararosaniline base and alpha-naphtholbenzein. The indicating agent is applied to a substrate which is then inserted into a tube or straw, which can be attached to the inlet of a breath collection balloon. When the patient blows into the tube or straw, the indicating agent will change color if it detects levels of ammonia which are consistent with helicobacter pylori urease infection.

PORTNER, VIRGINIA Docket Regular Amended (34 items, sorted by Mo-Old DESC, App # ASC)

Phx	App #	Status	Loc	Chrg To Loc	Class	Subclass	Class/Subclass	Title	Filed-to-Exnr	Unaval	Type	Mo-Old
	10/64555	71	e	e	435	007.320	435/007.320	DIAGNOSTIC METHODS	12/23/2005	false	-	2+
	10/770824	71	e	e	530	350.000	530/350.000	NOVEL PROTEINS FROM ACTINOBACILLUS PLEUROPNEUMONIAE	12/29/2005	false	-	2+
	10/451742	71	e	e	435	006.000	435/006.000	METHOD FOR DIAGNOSING ATROPHIC GASTRITIS	01/07/2006	false	-	2
	10/471914	71	e	e	435	006.000	435/006.000	ANTIBODIES FOR PREVENTING AND TREATING ATTACHING AND EFFACING ESCHERICHIA COLI (AEEC) ASSOCIATED DISEASES	01/11/2006	false	-	2
	10/687327	71	e	e	435	007.100	435/007.100	METHOD AND DEVICE FOR DETECTING AMMONIA ODORS AND HELICOBACTER PYLORI UREASE INFECTION	01/11/2006	false	-	2
	09/462682	71	e	e	424	190.100	424/190.100	PSEUDOMONAS EXOTOXIN A-LIKE CHIMERIC IMMUNOGENS	01/12/2006	false	-	2
	10/203679	71	e	e	435	007.320	435/007.320	METHOD FOR DETECTING HELICOBACTER PYLORI AND HEILMANNII IN FECAL AND SALIVARY SPECIMEN AND BIOPSY MATERIAL	01/12/2006	false	-	2
	10/729039	71	e	e	530	350.000	530/350.000	SOLUBLE RECOMANANT BOTULINUM TOXIN PROTEIN COMPOSITIONS	01/18/2006	false	-	2
	10/280130	71	e	e	514	012.000	514/012.000	USE OF EGF TO INHIBIT PATHOGENIC INFECTIONS	01/27/2006	false	-	1+

Org Lett. 2002 Mar 21;4(6):917-9.

Related Articles, Links



Photoreduction of benzophenones by amines in room-temperature ionic liquids.

Reynolds JL, Erdner KR, Jones PB.

Department of Chemistry, Wake Forest University, 115-A Salem Hall, Winston-Salem, North Carolina 27109, USA.

[reaction: see text] The amine-mediated photoreduction of benzophenones in room temperature ionic liquids was investigated. Unlike the analogous reaction in organic solvents, the photoreduction produces mainly the corresponding benzhydrol in most cases. Because the reaction consumes only 1 equiv of amine and the solvent can be easily recycled, the photoreduction allows a very clean method for the conversion of benzophenones to benzhydrols.

PMID: 11893185 [PubMed]

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L2: Entry 10 of 42

File: USPT

Dec 31, 1985

DOCUMENT-IDENTIFIER: US 4562449 A

TITLE: Chromogenic dihydroquinazolines

Detailed Description Text (4):

A mixture of 1 mmole of 4,4'-bis(dimethylamino)benzophenone (Michler's ketone) and 1 mmole of (2-benzothiazolyl)-3-diethylaminophenylamine in 10 ml of phosphoroxo trichloride is heated to reflux for 1 1/2 to 2 hours. The reaction mixture is poured on ice, washed with a small amount of methanol, made alkaline with concentrated ammonia and stirred for 1 hour at room temperature. The precipitate is isolated by filtration and taken up in dichloromethane or toluene. The solution is dried over anhydrous sodium sulfate and chromatographed over 70 g of silica gel with a 10:1 to 5:1 mixture of toluene/ethyl acetate. The main fraction is recrystallised from methanol, affording 320 mg (58% of theory) of a compound of the formula: ##STR25## in the form of white crystals which melt at 141.degree.-142.degree. C. This colour former develops an intense blue colour on acid clay.

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3,132,178

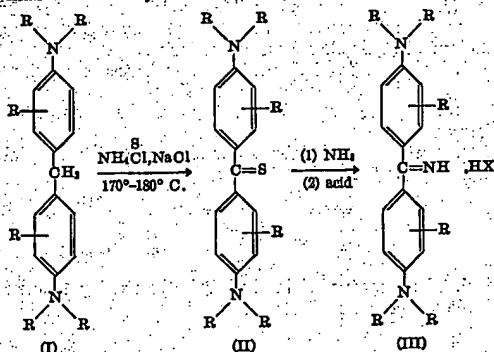
PROCESS FOR PREPARING AURAMINE USING UREA

Robert G. Weyker, North Plainfield, and Robert M. Yarrington and Samuel M. Gerber, Bound Brook, N.J., assignors to American Cyanamid Company, New York, N.Y., a corporation of Maine
No Drawing. Filed Apr. 4, 1961, Ser. No. 100,504
7 Claims. (Cl. 260-566)

This invention relates to an improved process for the preparation of auramine and its analogs. More specifically it provides for an increase in yield by the introduction of a novel constituent, a urea, into the reaction mixture.

Auramine and its analogs are among the best known dyes. They have been manufactured and sold in large quantities for many years. Its synthesis has become so well known as to be almost conventional. As a consequence, even a relatively small increase in yield is economically important.

The procedure which is conventionally employed in its manufacture may be illustratively represented as follows:



wherein each of the "R" radicals is hydrogen or lower alkyl. In auramine (C.I. 41,000) which will be used herein to generically represent the class, R is methyl. In this process, the methane base (I), along with sulfur, ammonium chloride and common salt are heated in a reactor to temperatures of about 170°-180° C. Salt, which is present as a diluent, is used in large amounts. A thioether intermediate (II) is formed but not isolated. Anhydrous ammonia gas is simultaneously introduced into the heated reaction mixture whereupon the ketonimine is formed and later isolated as a salt, e.g., hydrochloride, by salting out from aqueous solution to give the desired auramine dyestuff.

The present invention is based on the discovery that increased yields are obtained by carrying out the preparation of these auramine dyestuffs in the presence of urea. It is conveniently added to or substituted for at least a part of the salt customarily employed. The term "urea" is used to designate the suitable urea compounds which include urea itself and symmetrical di- (lower alkyl) ureas, e.g., N,N'-dimethyl urea, N,N'-diethyl urea, N,N'-dipropyl urea, N,N'-dibutyl urea, N,N'-diamyl urea, and N,N'-dihexyl urea. In view of its low cost and availability, urea itself, is perhaps preferable for the purposes of this invention.

In the conventional process, from 7 to 10 parts of salt per part of the methane base ordinarily are used. In the process of this invention, all or a part of the salt is replaced by a urea compound. As a minimum, at least about 0.7 part of the urea per part by weight of the methane base should be used. The urea used may replace about an equal or greater weight of the salt ordinarily used. Thus, it may be stated that at least about 10% of

2

the salt ordinarily used in the reaction may be replaced either by urea or one of the symmetrical N,N'-di- (lower alkyl) ureas discussed above. Of course, the use of common salt may be entirely eliminated by replacing it with an equal or less than equal weight of urea, in which case the reaction is conducted in the presence of from about seven to about ten parts of urea by weight of the methane base.

Yields which are obtained by the use of the process of this invention range from about 12% to about 20% greater than those obtained from the prior art process. Thus, in an efficient laboratory operation, the prior art process results in yields of about 61% based on the methane base. Using similar conditions, in the process of this invention using a urea, this yield may be increased to up to about 75%.

Use of a urea in accordance with the process of the present invention should not be confused with the older practice of reacting tetramethyldiaminobenzophenone with urea, in the presence of a condensation catalyst to form auramine, as in German Patent 31,936. As there disclosed, auramine is prepared by reacting tetramethyldiaminobenzophenone with urea at 160° to 180° C., in the presence of zinc chloride. Urea is the main reactant, supplying the -NH radical in the final auramine product. Auramine also is known to result from reacting Michler's ketone with urea, and zinc chloride used in place of ammonium chloride. In that case, the mixture of urea and zinc chloride on heating, yields ammonium chloride, the reactant of the above-noted conventional operation.

The present invention is further illustrated by the following illustrative examples. Therein parts and percentages are based on parts by weight.

Example 1

To a jacketed, cylindrical kettle equipped with a close-fitting agitator is charged 1 part of tetramethyldiaminodiphenylmethane, 0.33 part of sulfur, 0.80 part of ammonium chloride, and 8.5 parts of urea-salt mixture containing 20% urea. Anhydrous ammonia gas is blown through the charge which is maintained at 170° C. After 6 hours, the reaction product is drowned in water and the product dye isolated by extraction with water. Auramine is obtained in a yield of 85% of theory, based on the weight of the methane base starting material.

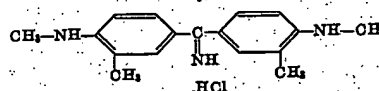
Example 2

To show the desirable effect on the yield by the addition of urea to the reaction mixture, the procedure of Example 1 was followed identically except that no urea was added to the reaction mixture, the urea being replaced by an equal weight of salt. The yield of 85% fell to only 61%.

Example 3

The procedure of Example 1 was followed identically, except for the substitution of 8.5 parts of an N,N'-dimethyl urea salt mixture containing 14% of the urea. The yield of auramine was about 80%.

Example 4



The procedure of Example 1 is followed except that bis-(4-methylamino-3-methylphenyl)methane is substituted for the methane base (tetramethyldiaminodiphenylmethane). The yield is similar to that of Example 1.

Example 5

The procedure of Example 1 is followed except that 8.5 parts of urea are used in place of the urea-salt mixture.

3

The yield of auramine is correspondingly high.

Example 6

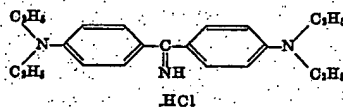
The procedure of Example 1 is followed except that the 8.5 parts of urea-salt mixture contains 90% urea. The yield of auramine is correspondingly high.

Example 7

The procedure of Example 1 is followed except that N,N-dimethyl - N'-N' - diethyldiaminodiphenylmethane is substituted for the methane base (tetramethyldiaminodiphenylmethane). A good yield of the corresponding analog of auramine is obtained.

No product was obtained when urea was omitted.

Example 8

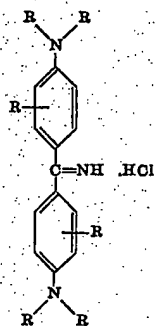


The procedure of Example 1 is followed except that tetraethyldiaminodiphenylmethane is substituted for the tetramethyldiaminodiphenylmethane and the proportion of the reactants are as follows: 1 part tetraethyldiaminodiphenylmethane, 0.26 part sulfur, 0.35 part NH_4Cl and 6.7 parts of a urea-salt mixture containing 20% urea. The yield of the corresponding ethyl analog of auramine is over about 70%.

This synthesis cannot be accomplished using the conventional 100% salt reaction medium since an unworkable tarry mass results. In the same manner, other tetra-alkyl analogs of auramine can be prepared in accordance with this invention as shown in this example using a reaction medium containing a urea compound.

We claim:

1. In the process for the preparation of a compound of the formula:



wherein R is individually selected from the group consisting of hydrogen and lower alkyl, by the reaction at an elevated temperature up to about 180°C . in an inert

4

reaction medium, of a p,p'-diaminodiphenylmethane of the formula:



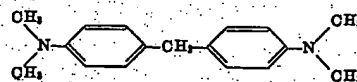
wherein R is as above defined, with sulfur and ammonium chloride and the after-treatment of the resulting reaction product with ammonia, the improvement wherein said reaction medium is a mixture of NaCl and at least 10% by weight of a member selected from the group consisting of urea and a symmetrical N,N'-di-lower alkyl-urea.

2. The process of claim 1 in which the member is present in an amount of at least 0.7 part by weight of the aminodiphenylmethane starting material.

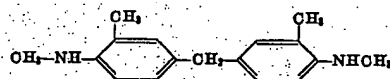
3. The process of claim 1 wherein a urea compound constitutes 20% of the reaction medium.

4. The process of claim 1 wherein the urea compound is urea.

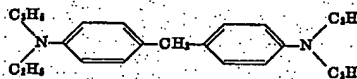
5. The process of claim 4 wherein the starting material is the compound of the formula:



6. The process of claim 4 wherein the starting material is the compound of the formula:



7. The process of claim 4 wherein the starting material is a compound of the formula:



References Cited in the file of this patent

Matsuo et al.: C.A., vol. 47, page 4915 (1953).
Endo et al.: C.A., vol. 52, page 13798 (1958).

DOCUMENT-IDENTIFIER: US 3132178 A

.TITLE: Process for preparing auramine using urea

OCR Scanned Text (1):

3 @ 1 3 2 9 1 7 8 Uni'ted States Patent Office 3' 132,178 PROCESS FOR PREPARING AURAM[NE USING UREA Robert G. Weyker, North Plainfield, and Robert M. Yar- rington and Samuel M. Gerber, Bound Brook, N.J., 5 assignors to American Cyanamid Company, New York, N.Y., a corporation of Maine NoDrawing. Filed Apr. 4, 1961, Ser. No. 100,504 7 Claims. (Cl. 260-566) This invention relates to an improved proress for the 1 0 preparation of auramine ind its analogs. More speci- fically it provides for an increase in yield by the intro- duction of a novel constituent, a urea, into the reactioii mixture. Auramine and its analogs are among the best known 1,5 dyes. They have been manufactured and sold in large quantities for many years. Its synthesis has become so well known as to be almost conventional. As a conse- lquerice, even a relatively small increase in yield is eco- nomi.cally important. 20 The prcedure which is conventionally employed in its manufacture may be illustratively represented as follows: R R R R R \NI \NI \NI 25 R R R s NH₄Cl, NaOl (1) Nlr3 170'@180' 0. (2) acid R R 35 \p R R R R (I) (II) (III) wherein each of the "R" radicals is hydrogen or lower 40 alkyl. In auramine (C.I. 41,000) which will be used here-in to generically represent. the class, R is methyl. In this process, the methane base (I), along with sulfur, ammoniurn chloride and common salt are heated in a reactor to temperatures of about 170'-180' C., Salt, which 's 4,5 present as a diluent, is used in large amounts. A thioketone intermediate (11) is f-ormed but not isolated. Anhydrous ammoma gas is simultaneously introduced into the heated reaction mixture whereupon the ketonin-iine is formed and later isolated as a salt, e.g., hydrochloride@, by 5(salting out from aqueous solution to give the desired auramine dyestuff . The present invention is based on the discovery that increased yields are obtained by carrying out the prepara- tion of these aurainine dyestuffs in the presence of urea. gr. It is conveniently added to or substituted for at least a part of the salt customarily employed. The term "urea@" is used to designate the suitable urea compounds which include urea itself and symmetrical di- (lower alkyl) ureas, e@g., N,N'-dimethyl urea, N,N'-diethyl urea, N,N'- 60 dipropyl urea, N,N'-dibutyl urea, N,N'-diamyl urea, and N,N'-dihexyl urea@ In view of its low cost and availabil- ity, urea itself, is perhaps preferable for the purposes of this invention. In the conventional process, from 7 to 10 parts of salt 65 per part of the methane base ordinarily are used. In the process of this invention, all or a part of the salt is re- placed by a urea compound@ As a miniinum, at least about 0.7 part of the urea per part by weight of the meth- ane base should be used. The urea used may replace about an equal or greater weight of the salt ordinarily ' o used. Thus, it may be stated that at least about 10% of P a t e n t e d M a y 5 , 1 9 6 4 2 the salt ordinarily used in the reaction may be replaced either by urea or one of the symmetrical N,N'-di (lower allcyl) ureas discussed above. Of course, the use of com'moiu salt may be entirely eliminated by replacing it with an equal or less than equal weight of urea, in which case the reaction is conducted in th6 presence of from about seven to about ten parts of urea by weight of the methane base. Yields which are obtained by the use of the process of this - mvehtion range from about 12% to about 20% greater than those obtained from the prior art process. Thus, in an efficient laboratory operation, the pnor art process results in yields of about 61% based on the methane base. Using siniilar conditions, in the process of this in.vention using a urea, this yield inay be increased to up to ab6ut 75%. Use of a urea in accordance with the process of the present invention should not be confused with the older practice of reacting tetramethyldiaminobenzophenone with urea, in the presence of a condensation catalyst to for . , as in German Patent 31,936. As the m auramine re disclosed, auramine is prepared by reacting tetramethyldiaminobenzophenone with urea at 160' to 180' C., in the presence of zinc chloride. Urea is the main reactant, supplying the -NH radical in the final auraniine product. Auramine also is known to result from reacting Michler's ketone with urea, and zinc chloride used in place of amrnonium chloride. In that case, the mixture of urea and zinc chloride on heating, yields ammonium chloride, the The present invention is further iflustrated by the following illustrative examples. Therein parts and percent- ages are based on parts by weight. Example 1 To a jacketed, cylindrical kettle equipped with a

closefitting agitator is charged 1 part of tetramethyldiaminodiphenylmethane, 0.33 part of sulfur, 0.80 part of ammonium chloride, and 8.5 parts of urea-salt mixture containing 20% urea. Anhydrous ammonia gas is blown through the charge which is maintained at 170° C. After 6 hours, the reaction product is drowned in water and the product dye isolated by extraction with water. Auramine is obtained in a yield of 85% of theory, based on the weight of the methane base starting material. Example 2 H₂NH IX 30 reactant of the above- noted conventional operation. To show the desirable effect on the yield by the addition of urea to the reaction mixture, the procedure of Example 1 was followed identically except that no urea was added to the reaction mixture, the urea being replaced by an equal weight of salt. The yield of 85% fell to only 61%. Example 3 The procedure of Example 1 was followed identically, except for the substitution of 8.5 parts of an N,N'-dimethyl urea salt mixture containing 14% of the urea. The yield of auramine was about 80%. Example 4 -<:- NH-CH₃ NH CH₃ CB@ HCl The procedure of Example 1 is followed except that bis-(4-methylamino-3-methylphenyl)methane is substituted for the methane base (tetramethyl-diaminodiphenylmethane). The yield is similar to that of Example 1. Example 5 The procedure of Example 1 is followed except that 8.5 parts of urea are used in place of the urea-salt mixture

Abstract Paragraph:

The invention provides a breath testing device which visually indicates the presence of ammonia in a patient's breath, in particular ammonia from helicobacter pylori urease infection. The breath testing device comprises a visual indicating agent which changes color in response to ammonia odors, such as 4,4'-bis(dimethylamino)-benzhydrol (Michler's hydrol or BDMB), pararosaniline base and alpha-naphtholbenzein. The indicating agent is applied to a substrate which is then inserted into a tube or straw, which can be attached to the inlet of a breath collection balloon. When the patient blows into the tube or straw, the indicating agent will change color if it detects levels of ammonia which are consistent with helicobacter pylori urease infection.

Summary of Invention Paragraph:

005720689 **IMAGE Available

Derwent Accession: 2004-543650

Non-specific sensor array detectors

Inventor: Steinthal, Gregory, INV

Sunshine, Steven, INV

Burch, Tim, INV

Plotkin, Neil, INV

Hsiung, Chang-Meng, INV

Assignee: Cyrano Sciences Inc.(02), Pasadena, CA

Correspondence Address: Foley & Lardner, 3000 K Street, N.W. Suite 500,
Washington, DC, 20007, US

	Publication Number	Kind	Date	Application Number	Filing Date
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Main Patent	US 20040135684	A1	20040715	US 2003624194	20030721
Provisional				US 60-397135	20020719

Fulltext Word Count: 15066

Description of the Invention:

...vapor based on the array pattern. The C320 has been successfully tested as a point **detector** for TICs (e.g., hydrazine, **ammonia**, formaldehyde, ethylene oxide, insecticides) as well as CWAs (e.g., GA, GB, HN-3, VX...and are excellent ink jetting candidates. Other useful ink-jetting materials include surface modified gold **nanoparticle** formulations and nanotube formulations...

Coating having colour indication

PATENT (CC, No, Kind, Date): EP 1097240 A1 010509 (Basic)
EP 1097240 B1 041229

WO 2000003035 000120

APPLICATION (CC, No, Date): EP 99933857 990712; WO 99US15599 990712

PRIORITY (CC, No, Date): US 113929 980710

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE

INTERNATIONAL PATENT CLASS (V7): C12Q-001/00; C12Q-001/02; C12Q-001/04;
C12M-001/00; A61B-005/15; C12M-001/24; G01N-033/483

NOTE:

No A-document published by EPO

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200453	2143
CLAIMS B	(German)	200453	1995
CLAIMS B	(French)	200453	2573
SPEC B	(English)	200453	6380
Total word count - document A			0
Total word count - document B			13091
Total word count - documents A + B			13091

1+5
12-5
12-5

...SPECIFICATION OF THE INVENTION

The present invention relates to a device according to claim 1, a kit according to claim 41 and a method according to claim 71 for detecting the presence...

...a further alternative embodiment of the sensor plate device;

FIG. 5 is an illustration of kit having a needle assembly for venipuncture and a vacuum sensor plate;

FIG. 6 is an...

...CLAIMS wherein said container is at a pressure of from 0 to 12 psi.

41. A kit of collecting a blood sample from a patient and detecting the presence of microorganisms in...

...provided as a wicking agent to draw liquid sample through the upper layer.

42. The kit of claim 41, wherein said container further comprises an adhesive layer between at least one...

...and the sensor layer, and b) the sensor layer and the container wall.

43. The kit of claim 41, wherein the sensor layer is opaque.

44. The kit of claim 41, wherein said immobilization layer comprises a gelling agent.

45. The kit of claim 44, wherein said gelling agent is at least one of a solid gel, a semi-solid gel, of a powdered gel.

46. The kit of claim 41, wherein said immobilization layer further comprises growth components for facilitating growth of microorganisms.

47. The kit of claim 41, wherein said container is a sealed container having a headspace above the immobilization layer.

48. The kit of claim 47, further comprising a gas permeable membrane in a wall of said container.

49. The kit of claim 48, further comprising a removable gas impermeable seal positioned proximate to said gas permeable membrane.

50. The kit of claim 41, wherein said wall of said container is transparent or translucent.

51. The kit of claim 41, wherein said sensor layer is capable of undergoing a localized change in the ultraviolet, visible, and/or

infrared spectrum.

52. The kit of claim 51, wherein said localized change is detectable through said wall of said container.

53. The kit of claim 41, wherein the sensor layer undergoes a detectable change in response to changes...

...oxygen, hydrogen, hydrogen sulfide, carbon dioxide, ammonia, organic acid, nitrogen dioxide and pH.

54. The kit of claim 53, wherein said detectable change is detectable in the infrared, ultraviolet or visible spectrums.

55. The kit of claim 5, wherein said sensor layer comprises an indicator having a change detectable by imaging, fluorescence or reflectance technology.

56. The kit of claim 55, wherein the sensor layer exhibits a change in fluorescence intensity or visible color over a pH range of about 5.0 to 11.0.

57. The kit of claim 41, wherein said immobilization layer comprises an immobilized sample with microorganisms therein.

58. The kit of claim 41, wherein said immobilization layer comprises a single gelling agent or a plurality of gelling agents.

59. The kit of claim 58, wherein said gelling agents comprises one or more agents selected from gums...

...celluloses, cellulose derivatives, polyethylene glycoles, polyethylene oxides, polyvinyl alcohols, dextrans, polyacrylamides and polysaccharides.

60. The kit of claim 58, wherein a first gelling agent is provided in an upper layer of...

...second gelling agent is provided in a lower layer of said immobilization layer.

61. The kit of claim 41, further comprising conditioning components proximate to or within said immobilization layer for improving microorganism detection capabilities.

62. The kit of claim 61, wherein said conditioning components comprise at least one of lytic agents, lytic enzymes, surfactants and components to neutralize growth inhibitors.

63. The kit of claim 41, wherein said sensor layer comprises silicone.

64. The kit of claim 41, wherein the sensor layer is constructed so as to undergo detectable localized changes which correspond to the presence of microorganism colonies in the immobilization layer.

65. The kit of claim 64, wherein the sensor layer is an opaque layer which changes from one color to a second color while remaining opaque in the presence of microorganisms.

66. The kit of claim 64, wherein at least one of the immobilization layer and the sensor layer are opaque.

67. The kit of claim 64, wherein at least one layer in the device has matrixes that adversely affect visualization of microorganism colonies.

68. The kit of claim 67, wherein said at least one layer includes said sensor layer.

69. The kit of claim 64, wherein the sensor layer sufficiently blocks the viewing of the test sample from the side of the sensor opposite from the immobilization layer.

70. The kit of claim 64, wherein the sensor layer blocks the viewing with the eye or detecting...

...blood sample from a patient and for detecting microorganisms in said blood sample with the kit of claim 41, comprising:

a) inserting a needle into a patient for withdrawing a blood...

...CLAIMS wenigstens einen Indikator, ausgewählt aus Fluorescein, Cumarin, Phenolphthalein, Thymolphthalein, Bromthymolblau, Thymolblau, Xylenolblau, o-Kresolphthalein und (α)- Naphtholbenzein , umfasst.

26. Sensorvorrichtung nach Anspruch 2, wobei die Sensorschicht eine Veränderung in Reaktion auf eine...

...Anspruch 1, wobei der Behälter unter einem Druck von 0 bis 12 psi steht.

41. Kit zum Sammeln einer Blutprobe von einem Patienten und zum Detektieren der Anwesenheit von Mikroorganismen in...

...Saugwirkung vorgesehen ist, um eine flüssige Probe durch die obere Lage zu ziehen, umfasst.

42. Kit nach Anspruch 41, wobei der Behälter ferner eine klebende Schicht zwischen wenigstens einem von a) der Immobilisierungsschicht und der Sensorschicht und b) der Sensorschicht und der Behälterwand umfasst.

43. Kit nach Anspruch 41, wobei die Sensorschicht lichtundurchlässig ist.

44. Kit nach Anspruch 41, wobei die Immobilisierungsschicht einen Gelbildner umfasst.

45. Kit nach Anspruch 44, wobei der Gelbildner wenigstens eines von einem festen Gel, einem halbfesten Gel, von einem pulverförmigen Gel ist.

46. Kit nach Anspruch 41, wobei die Immobilisierungsschicht ferner Kultivierungskomponenten zur Vereinfachung der Vermehrung von Mikroorganismen umfasst.

47. Kit nach Anspruch 41, wobei der Behälter ein versiegelter Behälter mit einem Kopfraum oberhalb der Immobilisierungsschicht ist.

48. Kit nach Anspruch 47, welcher ferner eine für Gase durchlässige Membran in einer Wand des Behälters umfasst.

49. Kit nach Anspruch 48, welcher ferner einen entfernbaren, für Gase undurchlässigen Verschluss, welcher sich benachbart zu der für Gase durchlässigen Membran befindet, umfasst.

50. Kit nach Anspruch 41, wobei die Wand des Behälters lichtdurchlässig oder transluzent ist.

51. Kit nach Anspruch 41, wobei die Sensorschicht in der Lage ist, eine lokalisierte Veränderung im ultravioletten, sichtbaren und/oder infraroten Spektrum zu durchlaufen.

52. Kit nach Anspruch 51, wobei die lokalisierte Veränderung durch die Wand des Behälters hindurch detektierbar ist.

53. Kit nach Anspruch 41, wobei die Sensorschicht eine detektierbare Veränderung in Reaktion auf Veränderungen bei einem oder mehreren von Sauerstoff, Wasserstoff, Schwefelwasserstoff, Kohlendioxid, Ammoniak, organischer Säure, Stickstoffdioxid und pH durchläuft.

54. Kit nach Anspruch 53, wobei die detektierbare Veränderung in den infraroten, ultravioletten oder sichtbaren Spektren detektierbar ist.

55. Kit nach Anspruch 5, wobei die Sensorschicht einen Indikator umfasst, welcher eine Veränderung zeigt, welche durch Bildgebungs-, Fluoreszenz- oder Remissionstechniken detektierbar ist.

56. Kit nach Anspruch 55, wobei die Sensorschicht eine Veränderung der Fluoreszenzintensität oder sichtbaren Farbe über einen pH-Bereich von ungefähr 5,0 bis 11,0 zeigt.

57. Kit nach Anspruch 41, wobei die Immobilisierungsschicht eine immobilisierte Probe mit Mikroorganismen darin umfasst.

58. Kit nach Anspruch 41, wobei die Immobilisierungsschicht einen einzelnen Gelbildner oder eine Mehrzahl von Gelbildnern umfasst.

59. Kit nach Anspruch 58, wobei die Gelbildner ein oder mehrere Mittel,

0005835471

Derwent Accession: 2004-756720

Chemical and biological agent sensor array detectors

Inventor: Steinthal, Gregory, INV

Sunshine, Steven, INV

Burch, Tim, INV

Plotkin, Neil, INV

Hsiung, Chang-Meng, INV

Assignee: Cyrano Sciences Inc.(02), Pasadena, CA, 91107

Smiths Detection - Pasadena, Inc.(02)

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WASHINGTON, DC, 20007, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	----	-----	-----
Main Patent	US 20040204915	A1	20041014	US 2003698042	20031029
CIP	PENDING			US 2003624194	20030721
Provisional				US 60-397135	20020719
Provisional				US 60-422301	20021029

Fulltext Word Count: 17874

Description of the Invention:

...of superior chemical sensing performance properties relative to most previously available systems. Sensing materials include **nanoparticle** composite sensors such as polymer composite sensors, sensors based on nanotubes, and sol-gel based...surface-modified colloidal metal particle sensors other than carbon black. These include surface-modified gold **nanoparticles** as chemical sensors similar to the surface-modified carbon blacks described above. Use of these...

...a monolayer on the metal surface. In the present invention, both traditional polymer modified gold **nanoparticles** and biopolymer modified gold **nanoparticles** may be used as resistance based chemical and biological sensors. The resistive read out provides...

...vapor based on the array pattern. The C320 has been successfully tested as a point **detector** for TICs (e.g., hydrazine, **ammonia**, formaldehyde, ethylene oxide, insecticides) as well as CWAs (e.g., GA, GB, HN-3, VX... formulations, such as formulations of surface-modified carbon black sensors, intrinsically conducting sensors, surface-modified **nanoparticle** metal sensors, and nanotube based sensors for ink jetting. Once a formulation exists, physical deposition...

...ink jetting candidates. Other useful ink-jetting materials and jettable formulations include surface modified gold **nanoparticle** formulations and nanotube formulations. Such formulations preferably have solid to solvent ratios in the range...

6050494 **IMAGE Available
Derwent Accession: 2003-493444
UTILITY

Use of id semiconductor materials as chemical sensing materials, produced and operated close to room temperature

Inventor: Besnard, Isabelle, Tübingen, FR
Vossmeier, Tobias, Esslingen, DE
Yasuda, Akio, Esslingen, DE
Burghard, Marko, Magstadt, DE
Schlecht, Ulrich, Stuttgart, DE

Assignee: Unassigned

Correspondence Address: William S Frommer; Frommer Lawrence & Haug, 745
Fifth Avenue, New York, NY, 10151, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050072213	A1	20050407	US 2002496380	20021126
PCT	WO 2002EP13309		20021126		
Priority				EP 2001128064	20011126

Fulltext Word Count: 11271

Abstract:

...1), a sensor medium (3) formed on the substrate, the sensor medium comprising one-dimensional **nanoparticles**, wherein the one-dimensional **nanoparticles** essentially consist of a semiconducting $A_{\text{sub}} \times B_{\text{sub}} \text{y}$ compound, e.g. V_{sub} ...

Summary of the Invention:

...the humidity from 0 to 50% relative humidity. Sadaoka, Y.; Sakai, Y.; Murata, Y. U.; **Sensors** and Actuators 1993, B 13-14, 420-423 report a similar behavior of an optical **sensor** based on calcein-poly(acrylonitrile) in the case of **ammonia detection**. The sensitivity increased when $I/I_{\text{sub}0}$ (optical intensity ratio) decreased from 0.95...

...tection, DM 189) deposited on a mass-sensitive device (Boeker, P.; Horner, G.; Rosler, S. **Sensors** and Actuators 2000, B 70, 37-42). The response to 100 ppm **ammonia** (in Hertz) is double at 20.000 ppm water (saturated, humidity) compared to the response...

6369151 **IMAGE Available

Derwent Accession: 2004-460456

UTILITY

Nanostructure sensor device with polymer recognition layer

Inventor: Star, Alexander, Albany, CA, US

Gabriel, Jean-Christophe P., Pinole, CA, US

Gruner, George, Los Angeles, CA, US

Assignee: Unassigned

Correspondence Address: BRIAN M. BERLINER;O'MELVENY & MYERS LLP, 400 SOUTH
HOPE STREET, LOS ANGELES, CA, 90071-2899, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050279987	A1	20051222	US 2003656898	20030905
Provisional				US 60-408547	20020905

Fulltext Word Count: 3105

Summary of the Invention:

...nanotubes grown on silicon or other substrates by chemical vapor deposition from iron-containing catalyst **nanoparticles** with methane/hydrogen gas mixture at 900 degree C. Other catalyst materials and gas mixtures...

Description of the Invention:

...shown in FIGS. 5A and 5B, respectively. The response and recovery of the PEI-functionalized **ammonia sensor** (FIG. 5B) are remarkably fast. The response to **ammonia** is also dependent on a gate voltage. At positive gate, measured current through the PEI...

Non-exemplary or Dependent Claim(s):

...9. The nanostructure **sensor** of claim 1, wherein the target species comprises **ammonia** and the polymer layer is PEI...

00314583

IMMOBILIZATION OF BIOLOGICALLY ACTIVE MATERIALS AND DIAGNOSTIC AGENTS IN
CROSS-LINKED POLY(ORGANOPHOSPHAZENES)
IMMOBILISATION DE SUBSTANCES ET D'AGENTS DE DIAGNOSTICS BIOLOGIQUEMENT
ACTIFS AU SEIN DE POLY(ORGANOPHOSPHAZENE) RETICULES

Patent Applicant/Assignee:

THE PENN STATE RESEARCH FOUNDATION,

Inventor(s):

ALLCOCK Harry R,

PUCHER Shawn R,

VISSCHER Karyn B,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9532736 A1 19951207

Application: WO 95US6854 19950531 (PCT/WO US9506854)

Priority Application: US 94251510 19940531

Designated States:

(Protection type is "patent" unless otherwise stated - for applications
prior to 2004)

AU CA JP KR NO AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 12609

Fulltext Availability:

Detailed Description

Detailed Description

... 8 having a temperature
of between about 250C and 370C.

As used herein, the term **nanoparticle** or
nanosphere typically refers to a particle, usually
a solid particle (as opposed to a capsule), of size
ranging from 10 to 1000 nm. In a preferred
embodiment, the **nanoparticle** is biodegradable,
biocompatible, has a size of less than 200 nm and
has a rigid...and those applications that do not
require high enzyme activity (for example, an assay
to **detect** urea as opposed to a method to convert
all urea to **ammonia**). For those applications, the
meaning of a "significant amount of enzyme
activity" must be considered...tract) or by
inhalation.

The polymers disclosed herein can be fabricated
into loaded microparticles or **nanoparticles** using
any appropriate method known to those skilled in
the art.

05681266 JICST ACCESSION NUMBER: 04A0020624 FILE SEGMENT: JICST-E

Composite Nanofiber Interface for Chemical and Biochemical Sensor

DING B (1); KIM J (1); SHIRATORI S (1)

(1) Keio Univ.

Denki Gakkai Kemikaru Sensa Kenkyukai Shiryo(Papers of Technical Meeting on
Chemical Sensor, IEE Japan), 2003, VOL.CHS-03,NO.56-86, PAGE.113-116,
FIG.8, REF.11

JOURNAL NUMBER: L2895BAU

UNIVERSAL DECIMAL CLASSIFICATION: 543.084 543.9:577.1

LANGUAGE: English COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Conference Proceeding

ARTICLE TYPE: Original paper

MEDIA TYPE: Printed Publication

...ABSTRACT: electrospinning of homogenous solution of poly(vinyl
alcohol)(PVA), poly(acrylic acid)(PAA) and TiO₂ **nanoparticles** . A
series of nanofiber samples with different concentration of PAA were
fabricated on the QCM...

...resonance frequency shift due to additional mass loading. The results
showed the sensing properties for **ammonia** gas were strongly affected
by the concentration of PAA in nanofibers. And the **sensor** was
suitable to **detect** the low concentration of **ammonia** gas. (author
abst.)

1016548 **Image available**

THE USE OF 1D SEMICONDUCTOR MATERIALS AS CHEMICAL SENSING MATERIALS,
PRODUCED AND OPERATED CLOSE TO ROOM TEMPERATURE
UTILISATION DE MATERIAUX SEMI-CONDUCTEURS UNIDIMENSIONNELS COMME MATERIAUX
DE DETECTION CHIMIQUE, PRODUITS ET EXPLOITES A UNE TEMPERATURE PROCHE
DE LA TEMPERATURE AMBIANTE

Patent Applicant/Assignee:

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, (For all designated states except: US)

Patent Applicant/Inventor:

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DE, DE (Residence), JP (Nationality), (Designated only for: US)
BURGHARD Marko, Max-Planck-Institute for Solid State Research,
Heisenbergstrasse 1, 70569 Stuttgart, DE, DE (Residence), DE
(Nationality), (Designated only for: US)
SCHLECHT Ulrich, Max-Planck-Institute for Solid State Research,
Heisenbergstrasse 1, 70569 Stuttgart, DE, DE (Residence), DE
(Nationality), (Designated only for: US)

Legal Representative:

HOFFMANN Jorg Peter (agent), Muller, Hoffmann & Partner, Patentanwalte,
Innere Wiener Strasse 17, 81667 Munchen, DE,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200346536 A1 20030605 (WO 0346536)
Application: WO 2002EP13309 20021126 (PCT/WO EP0213309)
Priority Application: EP 2001128064 200111

3982110

Derwent Accession: 1998-311345

Utility

REASSIGNED

C/ Method for determining bacteria contamination in food package
; PACKAGE LINING COMPRISES HYDROPHILIC POLYMER PERMEABLE TO GAS RELEASED BY
BACTERIA AND CONTAINS INDICATOR FOR VISIBLE DETECTION OF GAS

Inventor: Horan, Thomas J., 3111 Rowena Dr., Los Alamitos, CA, 90720

Assignee: Unassigned

Unassigned Or Assigned To Individual (Code: 68000)

Examiner: Tran, Lien (Art Unit: 132)

Combined Principal Attorneys: Coleman, Henry D.; Sudol, R. Neil

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 5753285	A	19980519	US 96720217	19960926
Continuation	Abandoned			US 95389296	19950216

Fulltext Word Count: 4586

Description of the Invention:

...green (Tetrabromo-m-cresolsulfonephthalein), cresol red
(o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue
(3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein (4-
alpha-(4-Hydroxy-1-naphthyl)benzylidene!-1(4H)-naphthalenone) and neutral
red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator
for the detection of ammonia produced by contaminating bacteria
comprises a mixture of potassium iodide, mercuric (III) iodide, sodium
borate...

erwent Accession: 2000-086559

Utility

REASSIGNED

C/ Method for determining deleterious bacterial growth in packaged food utilizing hydrophilic polymers

; STORING FOOD IN A PACKAGE HAVING HYDROPHILIC POLYMER LINING PERMEABLE TO WATER OR WATER VAPOR AND GAS RELEASED BY BACTERIA SUCH AS CARBON DIOXIDE, HYDROGEN SULFIDE, SUFLUR DIOXIDE, AMMONIA AND INDICATOR FOR ACID PRODUCED BY GAS AND WATER

Inventor: Horan, Thomas J., Los Alamitos, CA

Assignee: Stoltenberg, Herbert W.(04), CA

Stoltenberg, Ruben(04), CA

Laird, Edwin(04), CA

Thomas J. Horan Family Trust(02), CA

Horan, Thomas J Family Trust

Unassigned Or Assigned To Individual (Code: 55274 68000)

Examiner: Brouillette, Gabrielle (Art Unit: 171)

Combined Principal Attorneys: Sudol, R. Neil; Coleman, Henry D.; Sapone, William J.

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6149952	A	20001121	US 9879797	19980515

Fulltext Word Count: 7778

Summary of the Invention:

...m-cresolsulfonephthalein), Congo red, cresol red (o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue (3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein (4-[alpha-(4-Hydroxy-1-naphthyl)benzylidene]-1(4H)-naphthalenone) and neutral red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator for the detection of ammonia produced by contaminating bacteria comprises a mixture of potassium iodide, mercuric (III) iodide, sodium borate...

Derwent Accession: 2002-124156

Utility

C/ Aldehyde test strip

; PROTEINS, AMINES, COLOR INDICATOR, POLYMER, AND WATER CARRIER;
QUANTITATIVE ANALYSIS OF GLUTARALDEHYDE OR FORMALDEHYDE

Inventor: Wu, Wen H., Elkhart, IN

Assignee: Integrated Biomedical Technology, Inc.(02), Elkhart, IN

Integrated Biomedical Technology Inc (Code: 46982)

Examiner: Warden, Jill (Art Unit: 173)

Assistant Examiner: Cross, LaToya

Law Firm: Marshall, Gerstein & Borun

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6436716	A	20020820	US 2000583050	20000530

Fulltext Word Count: 9474

Summary of the Invention:

...bis [2,4-dinitrophenyl]-acetate, tropaeolin, thymol blue,
o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A, alpha
- naphtholbenzein , alizarin yellow GG, alizarin yellow R, and the like,
or mixtures thereof. The preferred indicators...

Non-exemplary or Dependent Claim(s):

...bis[2,4-dinitrophenyl]acetate, tropaeolin, thymol blue,
o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A,
alpha - naphtholbenzein , alizarin yellow GG, alizarin yellow R, and
mixtures thereof...

2/3,KWIC/9 (Item 1 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

01361572

Assay for aldehyde content

Test fur Aldehyde Gehalt

Essai pour proportion d'aldehyde

PATENT ASSIGNEE:

Integrated Biomedical Technology, Inc., (2598960), 2931 Moose Trail,
Elkhart, Indiana 46514, (US), (Applicant designated States: all)

INVENTOR:

Wu, Wen H., 51819 Winding Waters Lane, Elkhart, Indiana 46514, (US)

LEGAL REPRESENTATIVE:

Brown, John David (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22,
80336 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 1160569 A2 011205 (Basic)

EP 1160569 A3 020911

APPLICATION (CC, No, Date): EP 2001113204 010530;

PRIORITY (CC, No, Date): US 583050 000530; US 697374 001026

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS (V7): G01N-031/22; G01N-033/00; G01N-021/78

ABSTRACT WORD COUNT: 97

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200149	1702
SPEC A	(English)	200149	10768
Total word count - document A			12470
Total word count - document B			0
Total word count - documents A + B			12470

...SPECIFICATION bis(2,4-dinitrophenyl)acetate, tropaeolin, thymol blue,
o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A, **alpha -**
naphtholbenzein , alizarin yellow GG, alizarin yellow R, and the like, or
mixtures thereof. The preferred indicators...

...CLAIMS bis(2,4-dinitrophenyl)acetate, tropaeolin, thymol blue,
o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A,
alpha - naphtholbenzein , alizarin yellow GG, alizarin yellow R, and
mixtures thereof.

21. A method of determining aldehyde...

01129023

EVACUATED SENSOR DEVICE FOR DETECTING MICROORGANISMS IN BLOOD SAMPLES, AND METHOD THEREFOR

LUFTLEERER SENSOR ZUM NACHWEIS VON MIKROORGANISMEN IN BLUTPROBEN UND ENTSPRECHENDE METHODE

DISPOSITIF CAPTEUR SOUS VIDE PERMETTANT DE DETECTER DES MICRO-ORGANISMES DANS LES PRELEVEMENTS DE SANG, ET PROCEDE D'UTILISATION

PATENT ASSIGNEE:

bioMerieux, Inc., (3893251), 100 Akzo Avenue, Treyburn Durham, NC 27712, (US), (Proprietor designated states: all)

INVENTOR:

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JEFFREY, Scott, R., 12712 Victoria Woods Drive, Raleigh, NC 27613, (US)

HYMAN, Jones, M., 55 South Eagle Circle, Durham, NC 27703, (US)

THORPE, Thurman, C., 6713 Lipscomb Drive, Durham, NC 27712, (US)

LEGAL REPRESENTATIVE:

't Jong, Bastiaan Jacobus et al (49911), Arnold & Siedsma, Advocaten en Octrooigemachtigden, Sweelinckplein 1, 2517 GK Den Haag, (NL)

PATENT (CC, No, Kind, Date): EP 1097240 A1 010509 (Basic)

EP 1097240 B1 041229

WO 2000003035 000120

APPLICATION (CC, No, Date): EP 99933857 990712; WO 99US15599 990712

PRIORITY (CC, No, Date): US 113929 980710

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE

INTERNATIONAL PATENT CLASS (V7): C12Q-001/00; C12Q-001/02; C12Q-001/04; C12M-001/00; A61B-005/15; C12M-001/24; G01N-033/483

NOTE:

No A-document published by EPO

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200453	2143
CLAIMS B	(German)	200453	1995
CLAIMS B	(French)	200453	2573
SPEC B	(English)	200453	6380
Total word count - document A			0
Total word count - document B			13091
Total word count - documents A + B			13091

...CLAIMS wenigstens einen Indikator, ausgewählt aus Fluorescein, Cumarin, Phenolphthalein, Thymolphthalein, Bromthymolblau, Thymolblau, Xylenolblau, o-Kresolphthalein und (alpha)- Naphtholbenzein , umfasst.

26. Sensorvorrichtung nach Anspruch 2, wobei die Sensorschicht eine Veränderung in Reaktion auf eine...

04579891 JICST ACCESSION NUMBER: 00A0319862 FILE SEGMENT: JICST-E

Spectrophotometric FIA of total acid number in lubricant.

JONOSONO KEIKO (1); IMATO TOSHIHIKO (1); IMAZUMI NORIYUKI (2); YAGI JUN'ICHI (2)

(1) Kyushu Univ., Grad. Sch.; (2) Idemitsu Kosan Co., Ltd., Lubr. Dep.

Bunseki Kagaku, 2000, VOL.49, NO.3, PAGE.189-194, FIG.7, REF.10

JOURNAL NUMBER: F0008AAZ ISSN NO: 0525-1931 CODEN: BNSKA

UNIVERSAL DECIMAL CLASSIFICATION: 543.63-124 665.637

LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal

ARTICLE TYPE: Short Communication

MEDIA TYPE: Printed Publication

ABSTRACT: A spectrophotometric FIA method for the determination of the total acid number in a lubricant was proposed, which involved using an acid-base buffer solution prepared with a nonaqueous solvent. This method is based on measurements of the absorbance change of an indicator contained in the acid-base buffer solution, which is generated due to a neutralization reaction of acid in the lubricant with the buffer base. The sample (200 .MU.l or 20 .MU.l) injected into a stream of a nonaqueous solvent, toluene/H₂O/2-propanol (52/1/47 v/v%), was merged with a stream of tetrabutylammonium hydroxide (TBAOH) solution; the sample acid was then neutralized with TBAOH. An excess of TBAOH was merged with a stream of tetramethylguanidine (TMG) hydrochloric acid solution containing an indicator (. ALPHA .- naphtholbenzein), which had a similar pKa value to TMGvHCl in the present nonaqueous solvent. The reaction of the excess TBAOH with TMGvHCl gave rise to a composition change of the acid-base buffer solution, TMG-TMGvHCl. Since the indicator, . ALPHA .- naphtholbenzein , behaves similarly to the buffer component, the change in the ratio of TMGvHCl/TMG could be determined by a measurement of the absorbance change of the indicator. The absorbance changes at 680 nm (the wavelength at maximum absorbance of . ALPHA .- naphtholbenzein in basic form) were monitored with a spectrophotometric detector. Peak-shape signals were obtained for acid samples, and a linear relationship between the peak height and the concentration of the samples was found. The sensitivity of the proposed method for several kinds of acids was nearly identical irrespective of the acids. The proposed method was successfully applied to the determination of the total acid number in the lubricant with a sampling rate of 20 hr⁻¹. (author abst.)

DESCRIPTORS: acid value; spectrophotometry(analysis); lubricating oil; quantitative analysis(analytical chemistry); flow injection analysis; neutralization titration; buffer solution; indicator(reagent); comparative test; potentiometric titration; throughput

BROADER DESCRIPTORS: functional value; spectrochemical analysis; instrumental analysis; analysis(separation); analysis; oils; lubricant(machine); titration; chemical analysis; electrolytic solution ; solution(liquid); liquid; analytical reagent; reagent; test; electrometric titration; performance

CLASSIFICATION CODE(S): CC08034J; YF02071R

2/3,KWIC/11 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2006 American Chemical Society. All rts. reserv.

124288903 CA: 124(21)288903w JOURNAL

The color of .alpha.-naphtholbenzein and its pH-dependence. Part 4.
Benzeins

AUTHOR(S): Kallmayer, H.-J.; Lenze, U.

LOCATION: Fachrichtung Pharm. Chem., Univ. Saarlandes, Saarbruecken,
Germany,

JOURNAL: Pharmazie DATE: 1996 VOLUME: 51 NUMBER: 2 PAGES: 89-92

CODEN: PHARAT ISSN: 0031-7144 LANGUAGE: German

01787165

Coating having colour indicator

Beschichtungsmittel mit Farbumschlag

Revetement avec indicateur de couleur

PATENT ASSIGNEE:

Brillux GmbH & Co. KG, (4025370), Weseler Strasse 401, 48163 Munster,
(DE), (Applicant designated States: all)

INVENTOR:

Stach, Dirk, Dr., Riegestrasse 170, 45768 Marl, (DE)

Leusmann, Jan, Grauten Ihl 80a, 48301 Nottuln, (DE)

LEGAL REPRESENTATIVE:

Cohausz & Florack (100241), Patent- und Rechtsanwälte Bleichstrasse 14,
40211 Dusseldorf, (DE)

PATENT (CC, No, Kind, Date): EP 1457529 A2 040915 (Basic)

EP 1457529 A2 040915

EP 1457529 A3 041208

APPLICATION (CC, No, Date): EP 2004005200 040304;

PRIORITY (CC, No, Date): DE 10310509 030308; DE 10310511 030309; DE
10318143 030418

DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR;
HU; IE; IT; LI; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK

INTERNATIONAL PATENT CLASS (V7): C09D-005/00; C09D-007/00

TRANSLATED ABSTRACT WORD COUNT: 38

ABSTRACT WORD COUNT: 72

LANGUAGE (Publication,Procedural,Application): German; German; German

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
----------------	----------	--------	------------

CLAIMS A	(German)	200438	507
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SPEC A	(German)	200438	1455
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Total word count - document A	1962
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Total word count - document B	0
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Total word count - documents A + B	1962
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...SPECIFICATION nach farblos bei niedrigerem pH.

Derartige Saure-Base-Indikatoren sind beispielsweise Phenolphthalein,
Nitramin, o-Kresolphthalein, (alpha)- Naphtholbenzein und
Thymolphthalein. Ein erfindungsgemas besonders geeigneter
Saure-Base-Indikator ist Phenolphthalein.

Der Saure-Base-Indikator...

...CLAIMS der Saure-Base-Indikator ausgewählt ist aus der Gruppe bestehend
aus Phenolphthalein, Nitramin, o-Kresolphthalein, (alpha)-
Naphtholbenzein und Thymolphthalein.

5. Beschichtungsmittel nach einem der vorangegangenen Anspruche, dadurch
gekennzeichnet, dass der Saure-Base...

4417092

Derwent Accession: 2000-086559

Utility

REASSIGNED

C/ Method for determining deleterious bacterial growth in packaged food utilizing hydrophilic polymers
; STORING FOOD IN A PACKAGE HAVING HYDROPHILIC POLYMER LINING PERMEABLE TO WATER OR WATER VAPOR AND GAS RELEASED BY BACTERIA SUCH AS CARBON DIOXIDE, HYDROGEN SULFIDE, SULFUR DIOXIDE, AMMONIA AND INDICATOR FOR ACID PRODUCED BY GAS AND WATER

Inventor: Horan, Thomas J., Los Alamitos, CA

Assignee: Stoltenberg, Herbert W.(04), CA

Stoltenberg, Ruben(04), CA

Laird, Edwin(04), CA

Thomas J. Horan Family Trust(02), CA

Horan, Thomas J Family Trust

Unassigned Or Assigned To Individual (Code: 55274 68000)

Examiner: Brouillette, Gabrielle (Art Unit: 171)

Combined Principal Attorneys: Sudol, R. Neil; Coleman, Henry D.; Sapone, William J.

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6149952	A	20001121	US 9879797	19980515

Fulltext Word Count: 7778

Summary of the Invention:

...m-cresolsulfonephthalein), Congo red, cresol red
(o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue
(3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein
(4-[alpha-(4-Hydroxy-1-naphthyl)benzylidene]-1(4H)-naphthalenone) and
neutral red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator for the detection of ammonia produced by contaminating bacteria comprises a mixture of potassium iodide, mercuric (III) iodide, sodium borate...

Utility

REASSIGNED

C/ Method for determining bacteria contamination in food package
; PACKAGE LINING COMPRISES HYDROPHILIC POLYMER PERMEABLE TO GAS RELEASED BY
BACTERIA AND CONTAINS INDICATOR FOR VISIBLE DETECTION OF GAS

Inventor: Horan, Thomas J., 3111 Rowena Dr., Los Alamitos, CA, 90720

Assignee: Unassigned

Unassigned Or Assigned To Individual (Code: 68000)

Examiner: Tran, Lien (Art Unit: 132)

Combined Principal Attorneys: Coleman, Henry D.; Sudol, R. Neil

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 5753285	A	19980519	US 96720217	19960926
Continuation	Abandoned			US 95389296	19950216

Fulltext Word Count: 4586

Description of the Invention:

...green (Tetrabromo-m-cresolsulfonephthalein), cresol red
(o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue
(3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein (4-
alpha-(4-Hydroxy-1-naphthyl)benzylidene!-1(4H)-naphthalenone) and neutral
red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator
for the detection of ammonia produced by contaminating bacteria
comprises a mixture of potassium iodide, mercuric (III) iodide, sodium
borate...

s ammonia? (100n) naphtholbenzein?

Your SELECT statement is:

s ammonia? (100n) naphtholbenzein?

Items	File
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Examined 50 files	
Examined 100 files	
Examined 150 files	
2	340: CLAIMS(R)/US Patent_1950-06/Mar 09
3	349: PCT FULLTEXT_1979-2006/UB=20060309,UT=20060302
Examined 200 files	
Examined 250 files	
4	654: US Pat.Full._1976-2006/Mar 09

3 files have one or more items; file list includes 299 files.

? save temp

Temp SearchSave "TI205019728" stored

? rf

Your last SELECT statement was:

S AMMONIA? (100N) NAPHTHOLBENZEIN?

Ref	Items	File
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N1	4	654: US Pat.Full._1976-2006/Mar 09
N2	3	349: PCT FULLTEXT_1979-2006/UB=20060309,UT=20060302
N3	2	340: CLAIMS(R)/US Patent_1950-06/Mar 09
N4	0	2: INSPEC_1898-2006/Mar W1
N5	0	5: Biosis Previews(R)_1969-2006/Mar W1
N6	0	6: NTIS_1964-2006/Feb W4
N7	0	8: Ei Compendex(R)_1970-2006/Mar W1
N8	0	9: Business & Industry(R)_Jul/1994-2006/Mar 13
N9	0	10: AGRICOLA_70-2006/Mar
N10	0	11: PsycINFO(R)_1887-2006/Mar W1

3 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

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? b n1 n2 n3;exs

14mar06 17:40:43 User228206 Session D2577.4
\$5.43 2.047 DialUnits File411
\$5.43 Estimated cost File411
\$0.53 TELNET
\$5.96 Estimated cost this search
\$6.50 Estimated total session cost 2.249 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 654:US Pat.Full. 1976-2006/Mar 09

(c) Format only 2006 Dialog

***File 654: IPCR/8 classification codes now searchable in 2006 records.**

For information about IC= index changes, see HELP NEWSIPCR.

File 349:PCT FULLTEXT 1979-2006/UB=20060309,UT=20060302

(c) 2006 WIPO/Univentio

***File 349: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.**

File 340:CLAIMS(R)/US Patent 1950-06/Mar 09

(c) 2006 IFI/CLAIMS(R)

***File 340: IPCR/8 classification codes now searchable in 2006 records.**

For important information about IC=index changes, see HELP NEWSIPCR.

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      Set  Items  Description
      ---  ----  -
Executing TI205019728
>>>SET HILIGHT: use ON, OFF, or 1-5 characters
      245065  AMMONIA?
      91     NAPHTHOLBENZEIN?
      S1      9  AMMONIA? (100N) NAPHTHOLBENZEIN?
? t s1/3,kwic/all
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1/3,KWIC/1 (Item 1 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6069614 **IMAGE Available
Derwent Accession: 2005-313979
UTILITY

Method and device for detecting ammonia odors and helicobacter pylori urease infection

Inventor: Boga, RameshBabu, Roswell, GA, US
MacDonald, John Gavin, Decatur, GA, US
Assignee: Kimberly-Clark Worldwide, Inc., (02)
Correspondence Address: DORITY & MANNING, P.A., POST OFFICE BOX 1449,
GREENVILLE, SC, 29602-1449, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050084977	A1	20050421	US 2003687327	20031016

Fulltext Word Count: 5747

Abstract:

[00000] The invention provides a breath testing device which visually indicates the presence of ammonia in a patient's breath, in particular ammonia from helicobacter pylori urease infection. The breath testing device comprises a visual indicating agent which changes color in response to ammonia odors, such as 4,4'-bis(dimethylamino)-benzhydrol (Michler's hydrol or BDMB), pararosaniline base and alpha-naphtholbenzein. The indicating agent is applied to a substrate which is then inserted into a tube...

...the tube or straw, the indicating agent will change color if it detects levels of ammonia which are consistent with helicobacter pylori urease infection.

Summary of the Invention:

...0009] The visual indicating agent is typically a dye which is color sensitive to ammonia odors, such as 4,4'-bis(dimethylamino)-benzhydrol (BDMB or Michler's hydrol (MH)), a...

...chemical structure to MH, a triamino-triphenyl-methanol dye such as pararosaniline base (PAB), alpha-naphtholbenzein or any other dye which has high sensitivity for ammonia. The dye may change color by fading to a lighter color, by deepening in color...

Description of the Invention:

...0061] The devices were tested by injecting known concentrations of

ammonia hydroxide into the straws to determine their sensitivity to ammonia odors. A color change (from blue 16 to colorless 18) was noticed and was clearly visible in the presence of ammonia odors...

...0062] The experiment was repeated using PAB-dye and alpha-naphtholbenzein dye instead of MH-dye. On exposure to ammonia odors, the dye-coated substrates were observed to change from red to colorless and from...

...of the indicating dye showed a clear difference between before and after the exposure to ammonia odors (~100 ppb). The level of detection of ammonia odor by either MH or PAB...

1/3,KWIC/2 (Item 2 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6053700
Derwent Accession: 2005-321639
UTILITY
Color changing correction fluid
Inventor: Kwan, Wing Sum Vincent, Chicago, IL, US
Zhu, Jiandong, Aurora, IL, US
Assignee: Unassigned
Correspondence Address: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER,
233 S. WACKER DRIVE, CHICAGO, IL, 60606, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050075419	A1	20050407	US 2004776860	20040211
Provisional				US 60-508095	20031002

Fulltext Word Count: 2701

Non-exemplary or Dependent Claim(s):
...ethylamine (TEA), 2-amino-2-methyl-1-propanol (AMP),
dimethylaminopropylamine (DMAPA), N,N-dimethylethanolamine (DMEA),
ammonia and mixtures thereof...

...the color changing pH indicator is selected from the group consisting of
phenolphthalein, thymolphthalein, p- naphtholbenzein , 4-nitrophenol,
3-nitrophenol, o-cresolphthalein, m-cresol red, thymol blue,
m-cresol purple and...

1/3,KWIC/3 (Item 3 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

4417092
Derwent Accession: 2000-086559
Utility
REASSIGNED
C/ Method for determining deleterious bacterial growth in packaged food
utilizing hydrophilic polymers
; STORING FOOD IN A PACKAGE HAVING HYDROPHILIC POLYMER LINING PERMEABLE TO
WATER OR WATER VAPOR AND GAS RELEASED BY BACTERIA SUCH AS CARBON DIOXIDE,

HYDROGEN SULFIDE, SUFLUR DIOXIDE, AMMONIA AND INDICATOR FOR ACID PRODUCED BY GAS AND WATER

Inventor: Horan, Thomas J., Los Alamitos, CA

Assignee: Stoltenberg, Herbert W.(04), CA

Stoltenberg, Ruben(04), CA

Laird, Edwin(04), CA

Thomas J. Horan Family Trust(02), CA

Horan, Thomas J Family Trust

Unassigned Or Assigned To Individual (Code: 55274 68000)

Examiner: Brouillette, Gabrielle (Art Unit: 171)

Combined Principal Attorneys: Sudol, R. Neil; Coleman, Henry D.; Sapone, William J.

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6149952	A	20001121	US 9879797	19980515

Fulltext Word Count: 7778

Summary of the Invention:

...m-cresolsulfonephthalein), Congo red, cresol red (o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue (3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein (4-[alpha-(4-Hydroxy-1-naphthyl)benzylidene]-1(4H)-naphthalenone) and neutral red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator for the detection of ammonia produced by contaminating bacteria comprises a mixture of potassium iodide, mercuric (III) iodide, sodium borate...

1/3,KWIC/4 (Item 4 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

3982110

Derwent Accession: 1998-311345

Utility

REASSIGNED

C/ Method for determining bacteria contamination in food package ; PACKAGE LINING COMPRISES HYDROPHILIC POLYMER PERMEABLE TO GAS RELEASED BY BACTERIA AND CONTAINS INDICATOR FOR VISIBLE DETECTION OF GAS

Inventor: Horan, Thomas J., 3111 Rowena Dr., Los Alamitos, CA, 90720

Assignee: Unassigned

Unassigned Or Assigned To Individual (Code: 68000)

Examiner: Tran, Lien (Art Unit: 132)

Combined Principal Attorneys: Coleman, Henry D.; Sudol, R. Neil

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 5753285	A	19980519	US 96720217	19960926
Continuation	Abandoned			US 95389296	19950216

Fulltext Word Count: 4586

Description of the Invention:

...green (Tetrabromo-m-cresolsulfonephthalein), cresol red

(o-Cresolsulfonephthalein), phenolphthalein, bromothymol blue (3',3"-Dibromothymolsulfonephthalein), p- naphtholbenzein (4-alpha-(4-Hydroxy-1-naphthyl)benzylidene)-1(4H)-naphthalenone) and neutral red (3-Amino...

...2 SO₄ production by contaminating bacteria). An exemplary indicator for the detection of ammonia produced by contaminating bacteria comprises a mixture of potassium iodide, mercuric (III) iodide, sodium borate...

1/3,KWIC/5 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01234381

COLOR CHANGING CORRECTION FLUID

LIQUIDE CORRECTEUR CHANGEANT DE COULEUR

Patent Applicant/Assignee:

SANFORD L P, 29 East Stephenson Street, Freeport, IL 61032, US, US
(Residence), US (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:

KWAN Vincent Wing Sum, 2909 South Wells, Chicago, IL 60616, US, US
(Residence), US (Nationality), (Designated only for: US)

ZHU Jiandong, 2367 Wilson Creek Circle, Aurora, IL 60504, US, US
(Residence), US (Nationality), (Designated only for: US)

Legal Representative:

HULL Michael R (agent), Marshall Gerstein & Borun LLP, 233 S. Wacker Drive, Suite 6300, Sears Tower, Chicago, IL 60606-6357, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200540290 A1 20050506 (WO 0540290)

Application: WO 2004US26118 20040812 (PCT/WO US04026118)

Priority Application: US 2003508095 20031002

Designated States:

(All protection types applied unless otherwise stated - for applications 2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 2609

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... tri-ethylamine (TEA), 2-aminomethyl-1-propanol (AMP), dimethylaminopropylamine (DMAPA), N,N-dimethylethanolamine (DMEA), ammonia and mixtures thereof.

In another refinement, a volatile acid is used which comprises acetic acid...

...selected from the group consisting of pentamethoxy red, inethyl red,

methyl yellow, phenolphthalein, thymolphthalein, p-naphtholbenzein, 4-nitrophenol, 3-nitrophenol, o-cresolphthalein, m-cresol red, thymol blue, m-cresol purple and...

...mixture. Further, a mixture of different amines can be advantageous. For example, the combination of ammonia which is a quickly evaporating amine with DMEA, which is slowly evaporating amine, can be...

...Preferred color changing pH indicators include pentamethoxy red, methyl red, methyl yellow, phenolphthalein, thymolphthalein, p-naphtholbenzein, 4-nitrophenol, 3-nitrophenol, o-cresolphthalein, m-cresol red, thymol blue, m-cresol...

Claim

... consisting of tri-ethylamine (TEA), 2-amino-2-methyl-1-propanol (AMP), dimethylaminopropylamine (DMAPA), N,N-dimethylethanolamine (DMEA), ammonia and mixtures thereof.

3 The color changing correction fluid of claim 1 wherein the color changing pH indicator is selected from the group consisting of phenolphthalein, thymolphthalein, p-naphtholbenzein, 4-nitrophenol, 3-nitrophenol, o-cresolphthalein, 1-m-cresol red, thymol blue, m-cresol...

1/3,KWIC/6 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01233619 **Image available**

VISUAL INDICATING DEVICE FOR BAD BREATH
DISPOSITIF D'INDICATION VISUELLE DE MAUVAISE HALEINE

Patent Applicant/Assignee:

KIMBERLY-CLARK WORLDWIDE INC, 401 N. Lake Street, Neenah, WI 54956, US,
US (Residence), US (Nationality), (For all designated states except:
US)

Patent Applicant/Inventor:

MACDONALD John Gavin, 1472 Knollwood Terrace, Decatur, GA 30033, US, US
(Residence), US (Nationality), (Designated only for: US)
HUANG Yanbin, 507 Belcourt Parkway, Roswell, GA 30076, US, US (Residence)
, CN (Nationality), (Designated only for: US)
MCGRATH Kevin Peter, 335 Hermitage Trail, Alpharetta, GA 30004, US, US
(Residence), US (Nationality), (Designated only for: US)
BOGA Ramesh Babu, 1214 Hemingway Lane, Roswell, GA 30075, US, US
(Residence), IN (Nationality), (Designated only for: US)

Legal Representative:

JOHNSTON Jason W (agent), Dority & Manning, P.A., P.O. Box 1449,
Greenville, SC 29602-1449, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200540794 A2-A3 20050506 (WO 0540794)
Application: WO 2004US27626 20040823 (PCT/WO US04027626)
Priority Application: US 2003687270 20031016

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO

SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 6903

Fulltext Availability:

Detailed Description

Detailed Description

... Indicating Agent for

Agent

Michler's Hydrol H (CH₃)₂NC₆H₅- (CH₃)₂NC₆H₆- Thiols, Mercaptans,

(MH) Ammonia , Amines,

Diamines and Polyamines

Pararosaniline (NH₂)C₆H₅- (NH₂)C₆H₅- (NH₂)C₆H₅- Ammonia , Amines,

Base (PAB) Diarnines and Polyamines

Ammonia , Arnines,

Alpha- C₆1 H 0 - 0

naphtholbenzein Diamines and Polyamines

(ANB)

Naphthochrome C₆1 NaO₂C C₀2Na Ammonia , Amines,

Green (NCG) HO 0 Diamines and Polyamines

I I I I

The dye may...

...will depend on the concentration of the indicating agent or the concentration of sulfur or ammonia compounds in the patient's breath.

Therefore, in order to observe a color change in response to sulfur and/or ammonia levels >10 parts per billion (ppb), more preferably >20 ppb, and most preferably >25 ppb...

1/3,KWIC/7 (Item 3 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00528079

METHOD FOR DETERMINING DELETERIOUS BACTERIAL GROWTH IN PACKAGED FOOD
UTILIZING HYDROPHILIC POLYMERS

PROCEDE PERMETTANT DE DETERMINER UNE CROISSANCE BACTERIENNE NEFASTE DANS
DES PRODUITS ALIMENTAIRES CONDITIONNES A L'AIDE DE POLYMERES
HYDROPHILES

Patent Applicant/Assignee:

THOMAS J HORAN FAMILY TRUST,

STOLTENBERG Herbert W,

STOLTENBERG Ruben J,

LAIRD Edwin C,

Inventor(s):

HORAN Thomas J DI,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9959431 A1 19991125

Application: WO 99US10537 19990512 (PCT/WO US9910537)

Priority Application: US 9879797 19980515

Designated States:

(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE
 GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK
 MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU
 ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH
 CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW
 ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 8036

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... m-cresolsulfonephthalein), Congo red, cresol
 red (o-Cresolsulfonephthalein), phenolphthalein, bromothymol
 blue (31,311-Dibromothymolsulfonephthalein), p- naphtholbenzein
 (4-[alpha-(4-Hydroxy-1-naphthyl)benzylidenel-1(4H)
 naphthalenone) and neutral red (3-Amino...

...from C02

or H2SO4 production by contaminating bacteria). An exemplary
 indicator for the detection of ammonia produced by contaminat
 ing bacteria comprises a mixture of potassium iodide, mercuric
 (III) iodide, sodium...

Claim

... group consisting of xylenol

blue, bromocresol purple, bromocresol green, cresol red,
 phenolphthalein, bromothymol blue, p- naphtholbenzein and
 neutral red.

18 A food storage package adapted to detect gas
 released by bacteria...

...the group consisting of carbon dioxide, carbon monoxide, hydrogen
 sulfide, sul

fur dioxide, hydrogen and ammonia gas, said hydrophilic
 polymeric composition either coating or containing an amount
 of an indicator effective...

1/3,KWIC/8 (Item 1 from file: 340)

DIALOG(R)File 340:CLAIMS(R)/US Patent

(c) 2006 IFI/CLAIMS(R). All rts. reserv.

10846261 2005-0084977 2005-0019974

C/METHOD AND DEVICE FOR DETECTING AMMONIA ODORS AND HELICOBACTER PYLORI
 UREASE INFECTION

Inventors: Boga RameshBabu (US); MacDonald John Gavin (US)

Assignee: Kimberly-Clark Worldwide Inc

Assignee Code: 42059

Attorney, Agent or Firm: DORITY & MANNING, P.A., POST OFFICE BOX 1449,
 GREENVILLE, SC, 29602-1449, US

	Publication Number	Kind	Date	Application Number	Date
Priority Applic:	US 20050084977	A1	20050421	US 2003687327	20031016
				US 2003687327	20031016

Abstract: The invention provides a breath testing device which visually indicates the presence of ammonia in a patient's breath, in particular ammonia from helicobacter pylori urease infection. The breath testing device comprises a visual indicating agent which changes color in response to ammonia odors, such as 4,4'-bis(dimethylamino)-benzhydrol (Michler's hydrol or BDMB), pararosaniline base and alpha-naphtholbenzein. The indicating agent is applied to a substrate which is then inserted into a tube...

...the tube or straw, the indicating agent will change color if it detects levels of ammonia which are consistent with helicobacter pylori urease infection.

1/3,KWIC/9 (Item 2 from file: 340)
 DIALOG(R) File 340:CLAIMS(R)/US Patent
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10836704 2005-0075419 2005-0017957
 C/COLOR CHANGING CORRECTION FLUID
 Inventors: Kwan Wing Sum Vincent (US); Zhu Jiandong (US)
 Assignee: Unassigned Or Assigned To Individual
 Assignee Code: 68000
 Attorney, Agent or Firm: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER,
 233 S. WACKER DRIVE, CHICAGO, IL, 60606, US

	Publication Number	Kind	Date	Application Number	Date
	US 20050075419	A1	20050407	US 2004776860	20040211
Priority Applic:				US 2004776860	20040211
Provisional Applic:				US 60-508095	20031002

Non-exemplary Claims:

...ethylamine (TEA), 2-amino-2-methyl-1-propanol (AMP),
 dimethylaminopropylamine (DMAPA), N,N-dimethylethanolamine (DMEA),
 ammonia and mixtures thereof...

...the color changing pH indicator is selected from the group consisting of phenolphthalein, thymolphthalein, p-naphtholbenzein, 4-nitrophenol, 3-nitrophenol, o-cresolphthalein, m-cresol red, thymol blue, m-cresol purple and...

? b 155

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$2.80 4 Type(s) in Format 3
$2.80 4 Types
$4.83 Estimated cost File654
$0.64 0.134 DialUnits File349
$4.80 3 Type(s) in Format 3
$4.80 3 Types
$5.44 Estimated cost File349
$1.23 0.070 DialUnits File340
$3.02 2 Type(s) in Format 62
$3.02 2 Types
$4.25 Estimated cost File340
OneSearch, 3 files, 0.548 DialUnits FileOS
$0.26 TELNET
$14.78 Estimated cost this search
$21.28 Estimated total session cost 2.798 DialUnits
  
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File 155:MEDLINE(R) 1951-2006/Mar 10

(c) format only 2006 Dialog

*File 155: Medline has been reloaded. Some accession numbers have changed.

Set	Items	Description
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? s berthelot?		
S1	87	BERTHELOT?
? s s1 and nanoparticl?		
87	S1	
5868	NANOPARTICL?	
S2	0	S1 AND NANOPARTICL?
? s nanoparticl?		
S3	5868	NANOPARTICL?
? s s3 and ammonia?		
5868	S3	
29516	AMMONIA?	
S4	20	S3 AND AMMONIA?
? t s4/9/all		

4/9/1

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

19881359 PMID: 16256655

Direct coating of gold nanoparticles with silica by a seeded polymerization technique.

Mine Eiichi; Yamada Akira; Kobayashi Yoshio; Konno Mikio; Liz-Marzan Luis M

Department of Chemical Engineering, Graduate School of Engineering, Tohoku University, Aoba, Aramaki-aza, Aoba-ku, Sendai 980-8579, Japan.

Journal of colloid and interface science (United States) Aug 15 2003, 264 (2) p385-90, ISSN 0021-9797--Print Journal Code: 0043125

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: PubMed not MEDLINE

Gold nanoparticles prepared through a conventional citrate-reduction method were directly coated with silica by means of a seeded polymerization technique based on the Stober method. The method required no surface modification. The addition of tetraethylorthosilicate and water prior to ammonia was found to be critical to obtain a proper coating. The silica shell thickness was varied from 30 to 90 nm for TEOS concentrations of 0.0005-0.02 M at 10.9 M of water and 0.4 M of ammonia. The optical spectra of the core-shell gold-silica composite particles agreed with predictions of Mie theory.

Record Date Created: 20051031

Record Date Completed: 20060209

4/9/2

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

19881358 PMID: 16256654

Low-temperature synthesis of niobium oxide nanoparticles from peroxo

niobic acid sol.

Uekawa Naofumi; Kudo Takuji; Mori Fumihiko; Wu Yong Jun; Kakegawa Kazuyuki

Department of Materials Technology, Faculty of Engineering, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba-shi 263-8522, Japan.
uekawa@faculty.chiba-u.jp

Journal of colloid and interface science (United States) Aug 15 2003,
264 (2) p378-84, ISSN 0021-9797--Print Journal Code: 0043125

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: PubMed not MEDLINE

A peroxo niobic acid sol was prepared by peptization of the niobic acid precipitate (Nb₂O₅.nH₂O) with a H₂O₂ aqueous solution. Crystallized Nb₂O₅ nanoparticles and niobic acid nanoparticles were obtained by heating the peroxo niobic acid sol. When peroxo niobic acid sol prepared by peptization of the niobic acid precipitate ([NH₃]=0.3 mol/l) was heated at 348 K for 1 week, Nb₂O₅ nanoparticles with a diameter of 4.5 nm and a S(BET) of 275 m²/g were obtained. When peroxo niobic acid sol prepared by peptization of the niobic acid precipitate ([NH₃]=1 mol/l) was heated at 348 K for 1 week, niobic acid nanoparticles with a diameter of less than 2 nm were obtained. The pore structure and degree of crystallinity of the nanoparticles prepared by heating the peroxo niobic acid sol greatly depended on the concentration of the ammonia solution used for preparing the niobic acid precipitate.

Record Date Created: 20051031

Record Date Completed: 20060209

4/9/3

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

19358699 PMID: 15913636

A novel method for synthesis of silica nanoparticles .

Rao Kota Sreenivasa; El-Hami Khalil; Kodaki Tsutomu; Matsushige Kazumi; Makino Keisuke

Venture Business Laboratory, Kyoto University, Yoshida-Honmachi, Sakyo-ku, Japan. kotas 1999@yahoo.com

Journal of colloid and interface science (United States) Sep 1 2005,
289 (1) p125-31, ISSN 0021-9797--Print Journal Code: 0043125

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Subfile: INDEX MEDICUS

A sequential method has been used, for the first time, to prepare monodisperse and uniform-size silica nanoparticles using ultrasonication by sol-gel process. The silica particles were obtained by hydrolysis of tetraethyl orthosilicate (TEOS) in ethanol medium and a detailed study was carried out on the effect of different reagents on particle sizes. Various-sized particles in the range 20-460 nm were synthesized. The reagents ammonia (2.8-28 mol L⁻¹), ethanol (1-8 mol L⁻¹), water (3-14 mol L⁻¹), and TEOS (0.012-0.12 mol L⁻¹) were used and particle size was examined under scanning electron microscopy and transmission electron microscopy. In addition to the above observations, the effect of temperature on particle size was studied. The results obtained in the present study are in agreement with the results observed for the electronic

absorption behavior of silica particles,

WEST Search History

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DATE: Tuesday, March 14, 2006

Hide?	Set Name	Query	Hit Count
		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	(michler\$ or bdmb or \$benzoylhydrol)	5171
<input type="checkbox"/>	L2	L1 same (ammonia! or nh3)	42
<input type="checkbox"/>	L3	L1 near10 (device or apparatus)	18

END OF SEARCH HISTORY

Chopra, et al. ("Carbon-nanotube-based Resonant-circuit Sensor for Ammonia," Applied Physics Letters, Volume 8, Number 24, 2002, which is incorporated herein in its entirety by reference thereto) have described an ammonia sensor formed of a simple micro-strip circular disk resonator coated with carbon nanotubes (either single-walled or multi-walled nanotubes) on the surface. The sensors show a shift in resonant frequency upon adsorption of ammonia of about 4.375 MHz for a single-walled nanotube (SWNT) sensor and a shift of about 3.25 MHz for a multi-walled nanotube (MWNT) sensor, and can detect the presence of ammonia down to a concentration of about 100 ppm...

DOCUMENT-IDENTIFIER: US 5904814 A

TITLE: Removal of water and ammonia from benzophenone imine reactor effluents

CLAIMS:

1. A process for removing water and ammonia from benzophenone imine reactor effluents resulting from the catalytic reaction of benzophenones of the formula I ##STR5## where R.sub.1 and R.sup.2, are independently selected from the group consisting of

a) halogen, hydroxyl, nitro, amino;

b) straight-chain, branched or cyclic alkyl or O-alkyl having from 1 to 12 carbon atoms, which may themselves be substituted with C.sub.6-10 -aryl, F, Cl, Br;

c) aryl or O-aryl having from 6 to 10 carbon atoms, which may themselves be substituted with C.sub.1-12 -alkyl or --O-alkyl;

d) heteroalkyl in which alkyl radicals defined as above are interrupted by one or more heteroatoms selected from the class consisting of O, S and N; and

e) heteroaryl having from 5 to 10 ring atoms including from 1 to 3 heteroatoms selected from the class consisting of O, S and N,

where m and n, independently, are integers from 0 to 5,

with ammonia,

which process comprises: distilling off the ammonia and removing the water by distillation or removing the water non-distillatively.

[Previous Doc](#) [Next Doc](#)

- c) aryl or O-aryl having from 6 to 10 carbon atoms, which may themselves be substituted with C₁₋₁₂-alkyl or —O-alkyl;
- d) heteroalkyl in which alkyl radicals defined as above are interrupted by one or more heteroatoms selected from the class consisting of O, S and N;
- e) heteroaryl having from 5 to 10 ring atoms including from 1 to 3 heteroatoms selected from the class consisting of O, S and N,

where m and n, independently, are integers from 0 to 5, with ammonia.

R¹ and R², independently of one another, are preferably hydroxyl, nitro, straight-chain or branched alkyl or O-alkyl having from 1 to 4 carbon atoms, or phenyl or O-phenyl, which may be unsubstituted or substituted with C₁₋₄-alkyl or C₁₋₄-O-alkyl.

m and n, independently, are preferably integers from 0 to 2, particularly preferably 0 or 1.

In particular, m=n=0, i.e. benzophenone is used for reaction with ammonia to give benzophenone imine.

The invention is illustrated below by means of examples.

The benzophenone imine reactor effluent used in the examples was obtained by the following process.

180 g of benzophenone and 720 g of ammonia per hour were passed, at a pressure of 200 bar and at 130° C., through a tubular reactor filled with 60 ml of titanium dioxide in the form of 3 mm extrudates. The aqueous phase was then separated off from the reactor effluent, and the organic phase was used in the following examples. This organic phase consisted of 89.8% by weight of benzophenone imine, 5.28% by weight of benzophenone, 1.82% by weight of water and 3.10% by weight of ammonia.

EXAMPLE 1

500 g of the benzophenone imine effluent were pumped continuously to a film evaporator with an oil temperature of from 100 to 120° C. and a pressure of 9 mbar. This gave, as bottom product, a total of 441 g of anhydrous, colorless benzophenone imine mixture having a content of 94.3% by weight of benzophenone imine and 5.68% by weight of benzophenone. The product had an APHA color number of 35 Hazen. The water content, determined by the Karl Fischer method, cf. DIN 51777, Part 1, direct method, was 0.03% by weight.

EXAMPLE 2

500 g of the benzophenone imine effluent were distilled continuously through a film evaporator with an oil temperature of from 160 to 180° C., at a pressure of less than 10 mbar. This gave, as product at the top of the column, a total of 422 g of anhydrous, colorless benzophenone imine mixture having a benzophenone imine content of 94.3% by weight and a benzophenone content of 5.56% by weight. The product had an APHA color number of 28 Hazen. The water content, determined by the Karl Fischer method, was 0.02% by weight.

EXAMPLE 3

250 g of the benzophenone imine effluent were pumped continuously to a falling-film evaporator with an oil temperature of 100° C., at a pressure of 40 mbar, to remove the ammonia. This gave, as bottom product, 228 g of ammonia-free raw benzophenone imine. This product had a water content of about 1.6% by weight, and was mixed with 47 g of molecular sieve (type 514, 4 Å), and stirred at room temperature. After 4 hours, the molecular sieve was filtered off, giving 214 g of colorless benzophenone imine mixture having a benzophenone imine content of 94.1% by weight

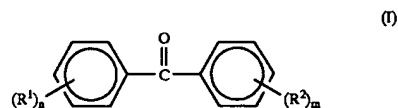
and a benzophenone content of 5.79% by weight. The APHA color number was 22 Hazen and the water content, determined by the Karl Fischer method, was 0.6% by weight.

In Examples 1 and 2, the ratio of benzophenone to benzophenone imine was equal to the ratio in the reactor effluent used, and in Example 3 it was slightly higher. This shows that during the work-up there is no, or only very little, reverse reaction or decomposition of the benzophenone imine. The novel process may therefore advantageously be used for purifying benzophenone imine reactor effluents in order to obtain a product which can be stored.

Benzophenone imine is used in industry as a starting compound for products which give protection from light.

We claim:

1. A process for removing water and ammonia from benzophenone imine reactor effluents resulting from the catalytic reaction of benzophenones of the formula I



where R₁ and R₂, are independently selected from the group consisting of

- a) halogen, hydroxyl, nitro, amino;
- b) straight-chain, branched or cyclic alkyl or O-alkyl having from 1 to 12 carbon atoms, which may themselves be substituted with C₆₋₁₀-aryl, F, Cl, Br;
- c) aryl or O-aryl having from 6 to 10 carbon atoms, which may themselves be substituted with C₁₋₁₂-alkyl or —O-alkyl;
- d) heteroalkyl in which alkyl radicals defined as above are interrupted by one or more heteroatoms selected from the class consisting of O, S and N; and
- e) heteroaryl having from 5 to 10 ring atoms including from 1 to 3 heteroatoms selected from the class consisting of O, S and N,

where m and n, independently, are integers from 0 to 5, with ammonia,

which process comprises: distilling off the ammonia and removing the water by distillation or removing the water non-distillatively.

2. The process of claim 1, wherein said ammonia and water are distilled off simultaneously.

3. The process of claim 1, wherein the ammonia is first distilled off from the reactor effluent and then the water is distilled off or removed non-distillatively.

4. The process of claim 3, wherein the non-distillative removal of the water is carried out with a drying agent.

5. The process of claim 3, wherein the ammonia is distilled using a falling-film evaporator.

6. The process of claim 5, wherein the water is removed using a molecular sieve.

7. The process of claim 1, wherein, before the distillation, the reactor effluent is separated by phase into an ammonia-containing aqueous phase and an organic phase, which still contains water and ammonia, and the aqueous phase is removed.

8. The process of claim 1, wherein the distillation is carried out in a stripping column or in a film evaporator.

9. The process of claim 1, wherein the distillation is carried out at from 20 to 200° C. and at a pressure of from 1 to 1000 mbar.

* * * * *

First Hit Fwd Refs

Lil: Entry 12 of 19

File: USPT

Nov 23, 2004

DOCUMENT-IDENTIFIER: US 6821786 B2

TITLE: Diagnostic test for elemental imbalances

Detailed Description Paragraph Table (1):

TABLE 1 Mineral Reagents Element Suitable Reagents Aluminum lumogallion; o,o'-dihydroxyazobenzene; aluminon; oxine Antimony 5-Br-PADAP; rhodamine B; brilliant green; thionalide Arsenic arsemate; thionalide; nitrocatechol; ethyl violet Barium dimethylsulfonazo-III; sulfonazo-III; chlorophosphonazo-III Beryllium chromazural S; arsenazo-I; acetylacetone; beryllon- III; 2-methyloxine; aluminon Bismuth bismuthio-II; XO; 5-Br-PADAP; DDTC; dithizone Boron azomethine-H; chromotropic acid; dinitronaphthalenediol; 3,5-di-t-butylcatechol; 2,6- dihydroxybenzoic acid; curcumin Bromine bindschedler's green leuco base; diphenylcarbazone Cadmium GHA; PAN; DDTC; cadion; dithizone; 5-Br-PADAP; 5-Br-DMPAP Calcium PC; MX; indo 1; indo 1-AM; chlorophosphonazo-III; neo-thorin; fluo 3; fluo 3-AM; arsenazo-III; HDOPP-Ca; rhod 2; rhod 2-AM; GHA; quin 2; quin 2-AM; calmagite; fura 2; fura 2-AM Cerium PAN; formaldoxime; pyrogallol red Cesium cesibor; tetraphenylborate Chlorine thio-michler's ketone; MQAE; SPQ; diethylcarbamate-Cu; diphenylcarbazone; triocytlin; tris(1,10-phenanthroline)Fe(II) Chromium 5-Br-PAPS; o-nitrophenylfluorone; diphenylcarbazide; 5-Br-PADAP Cobalt BTAMB; TAMSMB; 5-Cl-PADAB; dithizone; 3,5-diBr-PAMB; nitroso-DMAP; 5-Br-PADAP; nitroso-PSAP; nitroso-DEAP; 5-Br-PADAB Copper bathocuproin disulfonic acid disodium salt; bathocuproin; TAMSMB; 3,5-diBr-PAESA; sodium bicinchoninate; neocuproin; 5-Br-PSAA; BTAMB; TMPyP; Na-DDTC; dithizone Europium EuAc.sub.3 ; Eu.sub.2 O.sub.3 Fluorine alufusone; chromazurol S Gadolinium GdAc.sub.3 ; Gd(NO.sub.3).sub.2 Gallium lumogallion; sincon; oxine; rhodamine B; semiethylxylenol Blue Germanium phenylfluorone Gold KAUCN.sub.2 ; NaAuCl.sub.4 ; KAUCl.sub.4 ; KAUI.sub.4 ; rhodamine B; 5-(p-dimethylaminobenzylidene)rhodamine Indium PAN; PAR; oxine; dithizone Iodine K.sub.2 HgI.sub.4 /I.sub.2 ; bindschedler's green leuco base; diphenylcarbazone; tris(1,10-phenanthroline)Fe(II) complex Iridium K.sub.3 IrCl.sub.6 ; Na.sub.3 IrCl.sub.6 ; SnCl.sub.2 -HBr; leuco-crystal violet Iron bathophenanthroline disulfonic acid disodium salt; bathophenanthroline; nitroso-PSAP; TPTZ; PDT; nitro-PAPS; 3,5-diBr-PAMB; 5-Br-PSAA; PPKO; ferrene S; oxine Lead PbAc.sub.2 ; PbCl.sub.2 ; Pb(NO.sub.3).sub.2 ; MePbAc; TPPS; PAR; dithizone; DDTC Lithium thorin; bibenzyl-14-crown-4; phosphododecyl-14- crown4; TTD-14-crown-4; methyl dodecyl-12-crown-4; dibenzothiazolylmethane; oxine Manganese PAN; TAR; 1,10-phenanthroline; 2-methyloxine Mercury EtHgCl.sub.2 ; EtHgphosphate; Hg(CN).sub.2 ; EtHgthiosalicylate (thiomersal); mersalyl; PCMB; PHMB; PCMBs; PhHgAc; HgCl.sub.2 ; HgAc.sub.2 ; HgSO.sub.4 ; mercurochrome; Baker's reagent (2Hg); tetrakismercuryacetate (TAM) (4Hg); STTA; dithizone; thio-Michler's ketone; di- alpha-naphthylthiocarbonate Molybdenum PAR; oxine; DDTC; toluene-3,4-dithiol Nickel TAMSMB; BTAMB; PAN; 3,5-diBr-PAMB; dimethylglyoxime; 5-Br-PADAP Niobium PAR; sulfochlorophenol-S; TPAC; XO; BPR; oxine; phenylfluorone Nitrogen kalibor; phenol; pyradine-pyrazolone; o-phthalaldehyde; 4-aminonaphthalene-1-sulfonate; 4- hydroxyxoumarine; chromotropic acid; m- phenylenediamine Osmium Os(NH.sub.3).sub.6 I.sub.3 ; K.sub.2 OsCl.sub.6 ; K.sub.2 OsO.sub.4 ; bismuthio-II; tiron; PAR; TPAC; brilliant green Paladium K.sub.2 PdCl.sub.4 ; K.sub.2 PdBr.sub.4 ; K.sub.2 PdI.sub.4 ; PdCl.sub.2 ; Pd(NO.sub.3).sub.2 ; BTAMB; 5-Br-PSAA; 5-Br-PAPS; thiooxine; 5-Br- PADAP; rhodamine B; p-nitroso-N, N'dimethylaniline; thio-Michler's ketone Phosphorus Co(3)-5-Cl-PADAP; malachite green Platinum K.sub.2 PtCl.sub.4 ; K.sub.2 PtCl.sub.6 ; K.sub.2 PtI.sub.6 ; K.sub.2 Pt(NO.sub.2).sub.4 ; Pt(NH.sub.3).sub.2 Cl.sub.2 ; Pt(ethylenediamine)Cl.sub.2 ; K.sub.2 Pt(CN).sub.4 ; 5-Br-PAPS; dithizone; p-nitroso-

N,N'-dimethylaniline Potassium kalibor; bis(benzo-15-crown-5); 4TF; 6TF; picrylaminocrown; picrate; picrylamine; benzo-18-crown-6 Rhenium ReCl.sub.3 ; 2-furildioxime; dimethylglyoxime; methylene blue Rhodium 5-Br-PAPS; oxine; p-nitroso-N,N'-dimethylaniline Rubidium kalibor Ruthenium TPTZ; oxine; 1,10-phenanthroline; 5-Br-PAPS Samarium SmAc.sub.3 ; Sm(NO.sub.3).sub.3 ; SmCl.sub.4 Scandium chlorophosphonazo-III; PAN; BPR; 5,7-dichloro- oxine; quinizarin Selenium bismuthiol-2; 2,3-diaminonaphthalene; 3,3- diaminobenzidine; o-phenylenediamine; 4-chloro-o- phenylenediamine Silicon ammonium molybdate; malachite green Silver AgNO.sub.3 ; KAgCN.sub.2 ; 3,5-diBr-PADAP; 3,5-diBr- PAESA; 5-(p-dimethylaminobenzylidene rhodamine; 2- amino-6-methylthio-4-pyrimidine-carboxylic acid Sodium bis(12-crown-4); nitrophenylazo-15-crown-5; oxine Strontium PC; sulfonazo-III; dinitrosulfonazo-III; murexide Sulfur pararosaniline; barium chloranilate; methylene blue; O-phthalaldehyde; p-phenylenediamine; tris [2-(phenyliminomethyl)pyridinato]iron; 2-aminoperimidine HCl/HBr; Tellurium bismuthiol-2; diethyldithiocarbamate Thallium rhodamine B; malachite green; dithizone Thorium Th(NO.sub.3).sub.4 ; arsenazo-III; thorin; 5-Br-PADAP; morin Tin PV; SATP; toluene-3,4-dithiol; oxine; phenylfluorone Titanium diantipyrylmethane; tiron; BPR; 0,0'- dihydroxyazobenzene; crystal violet; alizarin Tungsten Na.sub.2 WO.sub.4 ; toluene-3,4-dithiol; oxine Uranium UO.sub.2 Ac.sub.2 ; K.sub.3 UO.sub.2 F.sub.5 ; UO.sub.2 (NO.sub.3).sub.2 ; UO.sub.2 SO.sub.4 ; arsenazo- III; PAN; 5-Br-PADAP; oxine Vanadium PAR; BPA; 5-Br-PAPS; oxine; 3,5-diBr-PADAP; 3,5- diBr-PAMB; 5-Br-PADAP Ytterbium TbCl.sub.3 ; YbAc.sub.3 Zinc zincon; 5-Br-PAPS; PAN; XO; TMPyP; zinquin ethyl ester; dithizone; T(5-St)P Zirconium Zr(NO.sub.3).sub.4 ; arsenazo-III; PV; TAN; XO; 5-Br-PADAP; morin; alizarin red S

CLAIMS:

6. The self-diagnostic test as described in claim 5 wherein the mineral specific reagents are selected from the group consisting of azomethine-H; chromotropic acid; dinitronaphthalenediol; 3,5-di-t-butylcatechol; 2,6-dihydroxybenzoic acid; curcumin; 5-Br-PAPS; nitrophenylfluorone; diphenylcarbazine; 5-Br-PADAP; BTAMB; TAMSMB; 5-Cl-PADAB; dithizone; 3,5-diBr-PAMB; nitroso-DMAP; nitroso-PSAP; nitroso-DEAP; 5-Br-PADAB; bathocuproin disulfonic acid disodium salt; bathocuproin; 3,5-diBr-PAESA; sodium bicinchoninate; neocuproin; 5-Br-PSAA; TMPyP; Na-DDTC; albusone; chromazurol S; phenylfluorone; K.sub.2 HgI.sub.4 /I.sub.2 ; bindschedler's green leuco base; diphenylcarbazon; tris(1,10-phenanthroline)Fe(II) complex; bathophenanthroline disulfonic acid disodium salt; TPTZ; PDTS; PDT; nitro-PAPS; PPKO; ferrene S; PAR; oxine; DDTC; toluene-3,4-dithiol; PAN; dimethylglyoxime; bismuthiol-2; 2,3-diaminonaphthalene; PV; SATP; toluene-3,4-dithiol; henylfluorone 3,3-diaminobenzidine; o-phenylenediamine; 4-chloro-o-phenylenediamine; ammonium molybdate; malachite green; BPA; zincon; XO; TMPyP; zinquin ethyl ester; and T(5-St)P.

8. The self-diagnostic test as described in claim 7 wherein the mineral specific reagents are selected from the group consisting of PC; MX; indo 1; indo 1-AM; chlorophosphonazo-III; neo-thorin; fluo 3; fluo 3-AM; arsenazo-III; HDOPP-Ca; rhod 2; rhod 2-AM; GHA; quin 2; quin 2-AM; calmagite; fura 2; fura 2-AM; thio-michler's ketone; MQAE; SPQ; diethylcarbamate-Cu; diphenylcarbazon; triocytlin; tris (1,10-phenanthroline)Fe(II); Co(3)-5-Cl-PADAP; malachite green; bis(12-crown-4); nitrophenylazo-15-crown-5; oxine; pararosaniline; barium chloranilate; methylene blue; O-phthalaldehyde; p-phenylenediamine; tris[2-(phenyliminomethyl)pyridinato] iron; and 2-aminoperimidine HCl/HBr.

10. The self-diagnostic test as described in claim 9 wherein the mineral specific reagents are selected from the group consisting of lumogallion; o,o'-dihydroxyazobenzene; aluminon; oxine; 5Br-PADAP; rhodamine B; brilliant green; arsemate; thionalide; nitrocatechol; ethyl violet; dimethylsulfonazo-III; sulfonazo-III; chlorophosphonazo-III; chromazurol S; arsenazo-I; acetylacetone; beryllon-III; 2-methyloxine; bismuthio-II; XO; DDTC; dithizone; bindschedler's green leuco base; diphenylcarbazon; PAN; formaldoxime; pyrogallol red-AM; cesibor

tetraphenylborate; EuAc.sub.3 Eu.sub.2 O.sub.3 ; GdAc.sub.3 ; Gd(NO.sub.3).sub.2 ;
✓ sincon; semiethylxylenol Blue; KAu(CN).sub.2 ; NaAuCl.sub.4 ; KAuCl.sub.4 ;
KAuI.sub.4 ; 5-(p-dimethylaminobenzylidene) rhodamine; PAR; K.sub.3 IrCl.sub.6 ;
Na.sub.3 IrCl.sub.6 ; SnCl.sub.2 -HBr; leuco-crystal violet; PbAc.sub.2 ;
PbCl.sub.2 ; Pb(NO.sub.3).sub.2 ; MePbAc; TPPS; thorin; bibenzyl-14-crown-4;
phosphododecyl-14-crown4; TTD-14-crown-4; methyl dodecyl-12-crown-4;
dibenzothiazolylmethane; EtHgCl.sub.2 ; EtHgphosphate; Hg (CN).sub.2 ;
EtHgthiosalicylate (thiomersal); mersalyl; PCMB; PHMB; PCMBS; PhEgAc; HgCl.sub.2 ;
HgAc.sub.2 ; HgSO.sub.4 ; mercurochrome; Baker's reagent (2Hg);
tetrakismercuryacetate (TAM) (4Hg); STTA; thio-Michler's ketone; di-alpha-
naphthylthiocarbonate; sulfochlorophenol-S; TPAC; BPR; phenylfluorone; Os
(NH.sub.3).sub.6 I.sub.3 ; K.sub.2 OsCl.sub.6 ; K.sub.2 OsO.sub.4 ; tiron; K.sub.2
PdCl.sub.4 ; K.sub.2 PdBr.sub.4 ; K.sub.2 PdI.sub.4 ; PdCl.sub.2 ; Pd
(NO.sub.3).sub.2 ; BTAMB; 5-Br-PSAA; 5-Br-PAPS; thiooxine; p-nitroso-
N,N'dimethylaniline; K.sub.2 PtCl.sub.4 ; K.sub.2 PtCl.sub.6 ; K.sub.2 PtI.sub.6 ;
K.sub.2 Pt(NO.sub.2).sub.4 ; Pt(NH3).sub.2 Cl.sub.2 ; Pt(ethylenediamine)Cl.sub.1 ;
K.sub.2 Pt(CN).sub.4 ; ReCl.sub.3 ; 2-furildioxime; dimethylglyoxime; methylene
blue; kalibor; TPTZ; 1,10-phenanthroline; SmAc.sub.3 ; Sm(NO.sub.3).sub.3 ;
SmCl.sub.4 ; 5,7-dichloro-oxine; quinizarin; AgNO.sub.3 ; KAgCN.sub.2 ; 3,5-diBr-
PADAP; 3,5-diBr-PAESA; 2-amino-6-methylthio-4-pyrimidine-carboxylic acid; PC;
dinitrosulfonazo-III; murexide; bismuthiol-2; diethyldithiocarbamate; malachite
green; Th(NO.sub.3).sub.4 ; arsenazo-III; morin; diantipyrylmethane; 0,0'-
dihydroxyazobenzene; crystal violet; alizarin; Na.sub.2 WO.sub.4 ; toluene-3,4-
dithiol; UO.sub.2 Ac.sub.2 ; K.sub.3 UO.sub.2 F.sub.5 ; UO.sub.2 (NO.sub.3).sub.2 ;
UO.sub.2 SO.sub.4 ; TbCl.sub.3 ; YbAc.sub.3 ; Zr(NO.sub.3).sub.4 ; PV; TAN; and
alizarin red S.

First Hit Fwd Refs

L11: Entry 16 of 19

File: USPT

Jun 27, 1995

DOCUMENT-IDENTIFIER: US 5428163 A

TITLE: Prodrugs for selective drug delivery

Brief Summary Text (56):

Methods of synthesis of quaternary ammonium salt poly methines appear in Appendix V.

Brief Summary Paragraph Table (2):

TABLE II _____ Dye Name or Structure; CI Name and Number; Other Names _____ Malachite Green 42000 Helvetia Green 42020 Basic Blue 1 42025 Brilliant Blue Setoglauanine Basic Green 1 42040 Brilliant Green Acid Blue 1 42045 Xylene Blue VS Patent Blue V Alphazurine 2G Acid Blue 3 42051 Brilliant Blue V Patent Blue V Food Green 3 42053 FDC Green 3 Acid Green 6 42075 Light Green SF Bluish Acid Blue 7 42080 Xylene Blue AS Patent Blue A Acid Green 3 42085 Acid Blue 9 42090 Erioglauanine Acid Green 5 42095 Light Green SF Yellowish Acid Green 9 42100 Erioviridene B Acid Blue 147 42135 Xylene Cyanol FF Basic Red 9 42500 Pararosalaniline Basic Violet 14 42510 Fuchsin Magenta Basic Fuchsin 42510B Basic Violet 2 42520 New Fuchsin New Magenta Hoffman Violet 42530 Iodine Violet Basic Violet 1 42535 Methyl Violet Basic Violet 13 42536 Methyl Violet 6B Basic Violet 3 42555 Crystal Violet Gentian Violet Iodine Green 42556 Basic Blue 8 42563 Victoria Blue 4R Acid Blue 13 42571 Fast Acid Violet 10B Acid Blue 75 42576 Eriocyanine A Methyl Green 42585 Ethyl Green 42590 Basic Violet 4 42600 Ethyl Violet Acid Violet 49 42640 Wool Violet 5BN Acid Blue 15 42645 Brilliant Milling Blue B Acid Violet 17 42650 Acid Violet 6B Wool Violet 4BN Formyl Violet Acid Violet 5BS Conc. Acid Violet 19 42685 Acid Fuchsin Red Violet 5R 42690 Acid Blue 22 42755 Aniline Blue Soluble Blue Solvent Blue 3 42775 Acid Blue 93 42780 Methyl Blue Aurin 43800 Mordant Blue 3 43820 Eriochrome Cyanine R Acid Green 16 44025 Naphthalene Green V Pontacyl Green NV Extra Basic Blue 11 44040 Victoria Blue R Basic Blue 15 44085 Night Blue Acid Green 50 44090 Wool Green S Kiton Green S Conc. Basic Green 3 Sevron Green B Brilliant Blue F & R Extra Brilliant Green Sulfonate _____ Hexakis(hydroxyethyl) Pararosalaniline ##STR20## New Green ##STR21## Phenolphthalein ##STR22## Malachite Green Ethiodide ##STR23## Hydroxyalkylated Pararosalanilines ##STR24## Hydroxyalkylated New Fuchsins ##STR25## New Yellow ##STR26## Doebner's Violet ##STR27## New Red ##STR28## Bis(hydroxyethyl) Doebner's Violet ##STR29## "New Magenta" ##STR30## Tetrakis(hydroxyethyl) Doebner's Violet ##STR31## Trichloro Crystal Violet ##STR32## Slow Red ##STR33## ##STR34## ##STR35## ##STR36## ##STR37## ##STR38## ##STR39## ##STR40## ##STR41## ##STR42## ##STR43## ##STR44## ##STR45## ##STR46## _____ Only the cyanide, bisulfite, and hydroxide ions are considered, regardless of the other anions present in the solution. More detailed descriptions of the compositions of photochromic materials tested are given in Macnair's review [255; tables 1A-4]. Ethanol. Diethyl ether. 1,2-Dichloroethane. 1,1-Dichloroethane, cyclohexane-1,1-dichloroethane, or cyclohexane-1,2-dichloroethane mixtures. Benzene. Dimethylsulfoxide, neat and aqueous. Acetone. Acetic acid. Ethyl acetate. Ethyl bromide. 2-Methoxyethanol. Chloroform. Ethanol with KCN. Ethanol with KOH. Carboxylic acids--acetic to stearic; hydrocinnamic acid; ethyl and butyl acid phthalates. Octadecylnitrile, tributyl phosphate, aniline, 2-(p-tert-butyl- phenoxy)ethanol, tetraethyleneglycol dimethyl ether, or poly(ethylene glycols). Amides--formamide to stearamide; methylformamide or methyl- acetamide; dimethyl- or diethyl-formamide or acetamide. Three-to-one solutions of cellulose acetate with any of the following five-to-one

plasticizer mixtures: Polyethylene Glycol butyl stearate, Polyethylene Glycol 600-butyl acetoxystearate, or Dowanol EP-butyl acetoxystearate. Water containing SO₂. Water containing bisulfite and papain. Poly(vinyl alcohol) with dimethylsulfoxide (5:1). Films, containing residual solvent, cast from the following solutions: ethanol-acetone solutions of vinyl acetate-vinyl alcohol copolymer; aqueous poly(vinyl alcohol); aqueous poly(vinyl pyrrolidone); or aqueous methyl vinyl ether-maleic acid copolymer. Methanol-dioxane with aqueous with aqueous NH₄HSO₃. Paper impregnated with a toluene solution of poly(methyl methacrylate), stearic acid, and 2-(p-tert-butylphenoxy)ethanol, then dried. Intramicellar impregnation of cellulose with the following swelling agents: n-propylamine, n-butylamine, n-hexylamine, 2-aminoethanol, dimethylformamide, acetic acid, dimethyl sulfoxide, methylacetamide, dimethylacetamide, or formamide. Films cast from an approximately 4:3 mixture of a 20% solution of cellulose acetate butyrate in toluene-ethyl acetate(1:1) and triallycyanurate in dioxane. Films cast from a 2:1 mixture of a 25% solution of cellulose acetate butyrate in toluene-ethyl acetate(1:1) and the titanium esters of N,N,N',N'-tetrakis(2-hydroxypropyl)ethylenediamine. Pure water. Films cast from aqueous gelatin or other hydrocolloids. Dimethylsulfoxide with methanolic KCN. 2-Methoxyethanol with methanolic KCN. Water or aqueous methanol containing bisulfite. Paper impregnated with m-dimethoxybenzene, acetonitrile, acetonitrile, acetic acid, or phenyl methyl carbinol. Ethanol-benzene. Aqueous ethanol, methanol, aqueous methanol, aqueous acetone, benzene-methanol, carbon tetrachloride-methanol, cyclohexane-methanol, or chloroform-methanol. Films cast from 3:1 solutions of cellulose acetate and either Polyethylene Glycol 600 .RTM. or ethylene glycol phenyl ether as plasticizer. Films, containing residual solvent, cast from solutions of either cellulose acetate in 2-methoxyethanol or poly(vinyl alcohol) in aqueous ethanol. Films, containing residual solvent, cast from solutions of either cellulose acetate butyrate in 2-methoxyethanol or poly(vinyl acetate) in methanol. Ethanol containing ammonia. Aqueous methanol containing NH₄HSO₃ and urease. Aqueous methanol containing NH₄HSO₃, with or without sodium dithionite. Aqueous acid at pH 1. Aqueous ammonia containing KCN. Paper impregnated with aqueous solutions with or without hydrocolloids. 2-Methoxyethanol containing HCl. Aqueous methanol containing NH₄HSO₃, and glucose oxidase. 9:1 Methanol-water. Aqueous NaOH.

Brief Summary Paragraph Table (3):

Photochromic Polymethine Dyes

.omega.-bis(p-Dimethylaminophenyl)polyenes Ar n	.alpha.,
	C.sub.6
H.sub.5 0, 1, 2 4-(CH.sub.3).sub.2 NC.sub.6 H.sub.4 0, 1, 2 4-(CH.sub.3).sub.2	
CHC.sub.6 H.sub.4 0, 1, 2, 3, 4 4-CH.sub.3 OC.sub.6 H.sub.4 0, 1, 2 4-C.sub.4	
H.sub.9 OC.sub.6 H.sub.4 0, 1, 2 3-CH.sub.3 C.sub.6 H.sub.4 1, 2 4-t-C.sub.4	
H.sub.9 C.sub.6 H.sub.4 1, 2 4-C.sub.2 H.sub.5 OC.sub.6 H.sub.4 1, 2 4-C.sub.5	
H.sub.11 C.sub.6 H.sub.4 1, 2 4-FC.sub.6 H.sub.4 1 4-F.sub.3 CC.sub.6 H.sub.4 1 2-	
(C.sub.6 H.sub.5).sub.2 NC.sub.6 H.sub.4 1 3,4-H.sub.2 N(OCH.sub.3)C.sub.6 H.sub.3	
1 2-Naphthyl 1, 2 4-ClC.sub.6 H.sub.4 2 2,4-Cl.sub.2 C.sub.6 H.sub.3 2 1-Naphthyl 2	
.alpha.-bis(p-dimethylaminophenyl)polyenes ##STR48## R R	.alpha.,

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##STR49## ##STR50## ##STR51## ##STR52## ##STR53## ##STR54## ##STR55## ##STR56##
##STR57## ##STR58## ##STR59## ##STR60## ##STR61## ##STR62##
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Miscellaneous polyenes ##STR63## ##STR64## ##STR65## ##STR66## ##STR67## ##STR68##
##STR69## ##STR70## ##STR71## ##STR72## ##STR73## ##STR74## ##STR75## ##STR76##
##STR77## ##STR78## ##STR79## ##STR80## ##STR81## ##STR82## ##STR83## ##STR84##
##STR85## ##STR86## ##STR87## ##STR88## ##STR89## ##STR90## ##STR91## ##STR92##
##STR93## ##STR94## ##STR95## ##STR96## ##STR97## ##STR98## SALT-ISOMERISM TYPE
PHOTOTROPIC DYES Night Blue ##STR99## Victoria Blue R ##STR100## Brilliant Milling

Blue B Brilliant Blue F & R Ex. Eriocyanine A ##STR101## Methyl Blue ##STR102##
 Aniline Blue ##STR103## Eriochrome Cyanine R ##STR104## Methyl Violet 6B ##STR105##
 Iodine Green ##STR106## Aniline Blue ##STR107## Wool Violet 5 BN ##STR108## Wool
 Violet 4 EM ##STR109## Light Green SF Yellowish ##STR110## Iodine Violet ##STR111##
 Methyl Violet ##STR112## Crystal Violet ##STR113## Ethyl Violet ##STR114## Acid
 Green L Extra ##STR115## Erioviridine B ##STR116## Light Green SF ##STR117##
 Victoria Green (Malachite Green) ##STR118## Red-Violet 5R ##STR119## Brilliant
 Green "B" ##STR120## Di-[4(N,N-diethylamino)phenyl]-[4-(N,N-diethyl- amine-2-
 methyl) phenyl] methyl carbonium ##STR121## Tri-[4(N,N-dipropylamino)phenyl] methyl
 carbonium ##STR122## Di-[4(N,N-diethylamino)phenyl]-[4(ethylamino)- phenyl] methyl
 carbonium ##STR123## Di-[4(N,N-diethylamino)phenyl]-[4(N,N-diethyl- amino)naphthyl]
 methyl carbonium ##STR124## Di-[4(N,N-dimethylamino)phenyl]-[4(hydroxy)phenyl]
 methyl carbonium ##STR125## Tri-[4(N-propylamino)phenyl] methyl carbonium
 ##STR126## Hectolene Blue DS-1398 Hectolene Blue DS-1823 Sevron Brilliant Red 4G
 Di-[4(N,N-dimethylamino)phenyl]-[4(hydroxy)phenyl] methyl carbonium ##STR127## Tri-
 [4(N-propylamino)phenyl] methyl carbonium ##STR128## Hectolene Blue DS-1398
 Hectolene Blue DS-1823 Sevron Brilliant Red 4G Genacryl Red 6B Genacryl Pink G
 Sevron Brilliant - Red B Sevron Brilliant - Red 3B 1,5-bis-[4(N,N-dimethylamino)
 phenyl]-1,5-bis- (phenyl)divinyl carbonium trifluoroacetate ##STR129## 1,1,3,3-
 tetrakis[4(N,N-dimethylamino)phenyl] vinyl carbonium perchlorate ##STR130## 1,5-
 bis-[4(N,N-dimethylamino)phenyl]-1,5-bis- (phenyl) divinyl carbonium p-
 toluenesulfonate ##STR131## 1,7-bis-[4(N,N-dimethylamino)phenyl]-1,7-bis- (2,4-
 dichlorophenyl) trivinyl carbonium perchlorate ##STR132## Di-[4(N,N-dimethylamino)
 phenyl vinyl]-[2,4-di- phenyl-6-methane thiopyran] methyl carbonium perchlorate
 ##STR133## 1,7-bis-[4-(N,N-dimethylamino)phenyl]-1,7-bis- (4-chlorophenyl) trivinyl
 carbonium trifluoroacetate ##STR134## 1,1,3-tris-[4-(N,N-dimethylamino)phenyl]
 divinyl carbonium perchlorate ##STR135## 1,1,7,7-tetrakis-[4-(N,N-dimethylamino)
 phenyl] trivinyl carbonium perchlorate ##STR136## 1,3-bis-[4-(N,N-dimethylamino)
 phenyl]-1,3-bis- (phenyl) vinyl carbonium perchlorate ##STR137## 1,1,5,5-tetrakis-
 [4-(N,N-dimethylamino)phenyl] divinyl carbonium perchlorate ##STR138## 1,5-bis-[4-
 (N,N-dimethylamino)phenyl]-1,5-bis- (phenyl) divinyl carbonium perchlorate
 ##STR139## 1,7-bis-[4-(N,N-dimethylamino)phenyl]-1,7-bis- (phenyl) trivinyl
 carbonium trifluoroacetate ##STR140## 1(1,3,3-trimethyl indoline)-2-[4-(N,N-
 dimethyl- amino)phenyl] ethylene carbonium perchlorate ##STR141## 1(1,3,3-trimethyl
 indoline)-4-[4-(N,N-dimethyl- amino)phenyl] butylene carbonium perchlorate
 ##STR142## 1,1,3,3-tetrakis-[4(N,N-diethylamino)phenyl] vinyl carbonium perchlorate
 ##STR143## 1,1-bis-[4-(N,N-diethylamino)phenyl]-3,3-bis- [4-(N,N-dimethylamino)
 phenyl] vinyl carbonium perchlorate ##STR144## 1,1,5,5-tetrakis-[4-(N,N-
 diethylamino)phenyl] divinyl carbonium perchlorate ##STR145## 1,1-bis-[4-(N,N-
 dimethylamino)phenyl]-3-[4-(amino) phenyl]-3-methylvinyl carbonium perchlorate
 ##STR146## Tris-[1,1-bis-[4(N,N-dimethylamino)phenyl] ethylene] methyl carbonium
 perchlorate ##STR147## Tris-[1,1-bis-[4-(N,N-diethylamino)phenyl] ethylene] methyl
 carbonium perchlorate ##STR148## 1,1,5-tris-[4-(N,N-dimethylamino)phenyl] divinyl
 carbonium perchlorate ##STR149## N[4-(N,N-dimethylamino) cinnamylidene] auramine
 ##STR150## 1,1-bis-[4-(N,N-dimethylamino)phenyl]-3,4-bis- (phenyl)]-3,4-diazo butene
 carbonium ##STR151## 1,1,5,5-tetrakis-[4-(N,N-dimethylamino)phenyl]- 2,3-diazo
 pentene carbonium ##STR152## N-(N',N'-dimethylamino cinnamylidene)-N,N-diphenyl
 ammonium ##STR153## Azo Polymethines Dyes of the general structural type ##STR154##
 ##STR155## ##STR156## Photochromic diazopolymethines

Detailed Description Text (148):

Method A. Michler's Ketone Method

Detailed Description Text (149):

To equal molar quantities of a p-amino benzophenone or di-(p-amino) benzophenone (Michler's type ketones) and aromatic amines, such as anilines and naphthyl amines, sufficient toluene-phosphorous oxychloride solution is added (3-5) to dissolve the reactants at 50.degree. C. The temperature is raised to 80.degree. C. and the solution is stirred for approximately 45 minutes or until the mass becomes very viscous. The sample is cooled and 10 ml of water added for each ml of phosphorous

oxychloride used, and heated to boiling. The solution is cooled and treated with 6N sodium hydroxide solution until the pH is 8 or more. The sample is steam-distilled to removed the last trace of any toluene or steam volatile unreacted amine. It is cooled and the aqueous phase poured off. The organic phase is dissolved in hot methanol-acetic acid (1:1) solution. The sodium salt of the anion for the dye form desired is then added. The sample is cooled and ether added slowly, while stirring to effect crystallization of dye.

Detailed Description Text (151):

Method B. Michler's Hydrol Method

Detailed Description Text (153):

Triphenylmethane type compounds may be produced by the condensation of a diphenyl substituted secondary alcohol and an aromatic ring. The secondary alcohol is of a type called Michler's hydrol of the general type formula: ##STR237## which is produced by the controlled reduction of the corresponding ketone with sodium amalgam in alcohol as a solvent. The hydrol is separated from an alcohol-water mixture, dried, and stored in a vacuum dessicator.

Detailed Description Text (196):

Sixty ml of a 3 molar etherial solution of methyl magnesium bromide was evaporated almost to dryness under reduced pressure in a 500 ml three-necked flask equipped with thermometer and nitrogen sparger. The grey moist residue was suspended in 75 ml of dry benzene. The flask was then equipped for refluxing by the addition of a condenser fitted with a CaCl₂ drying tube and an addition funnel. A 0.1 mole portion of the ketone dissolved in 250 ml of boiling benzene was then placed in the addition funnel and added dropwise to the warmed methyl magnesium bromide-benzene slurry over a half-hour period. The resulting reddish solution was refluxed for three hours. The termination of the reaction was indicated by the fading of the initial reddish color to a pale yellow. The reaction mixture was then cooled to room temperature and cautiously treated with 45 ml of saturated ammonium chloride solution. This mixture was filtered and the filtrate boiled with 0.1 g of p-toluenesulphonic acid until the evolution of water was completed. The acid contained in the reaction mixture was then removed by the addition of 0.5 g of sodium bicarbonate. The volume was reduced to one half by evaporation under reduced pressure. Five hundred ml of dry ethanol was added to the remaining solution, which was then allowed to cool with the subsequent precipitation of the ethylene compound. The precipitate was filtered, washed with 50 ml ice cold ethanol, and the crystals dried in a vacuum oven. Yield: 86 percent of theory: melting point 101.degree.-102.degree. C.

Detailed Description Text (217):

The position of the --N--N-- group in the carbon chain may be changed to occupy the 1 and 2 positions, as well as the above shown 2 and 3 positions, by using a secondary amine in place of B in the above series of reactions. With nitrogen atoms in the 1 and 2 positions, the 1 position nitrogen becomes a quaternary ammonium atom in one of the resonance states of the molecule.

Detailed Description Text (220):

Quaternary Ammonium Salt Polymethines

Detailed Description Text (221):

Three dyes of the type ##STR272## were prepared and tested for phototropy. ##STR273## N-(p-dimethylamino cinnamylidene)-N,N-diphenyl ammonium proved to be phototropic but broke down rapidly under ultraviolet light ##STR274## N-(p-dimethylamino cinnamylidene)-N,N-diethanol ammonium, and ##STR275## N-(p-dimethyl amino cinnamylidene) N,N-di-4(N,N-dimethylamino)phenyl ammonium were not phototropic.

Detailed Description Text (231):

Methyl magnesium bromide in ethyl ether is placed into a round bottom flask equipped with a condenser and an addition funnel. The ether is distilled off, and the methyl magnesium bromide then taken up with anhydrous benzene. A ketone is dissolved in anhydrous benzene and added dropwise to the Grignard reagent with continuous heating. After the addition is completed, the mixture is refluxed for three more hours. After cooling, sufficient ammonium chloride solution (saturated aqueous solution) is very carefully added in order to dissolve any free magnesium. The Grignard complex is decomposed with hydrochloric acid. After decomposition of the complex is complete, the solution is allowed to come to room temperature. After making sure the solution is alkaline to phenolphthalein, the benzene solution is decanted off of the solids. The solids are washed with two 50-ml portions of ether and the washings combined with the benzene solution. The ether-benzene solution is dried over anhydrous sodium sulfate.

183. JP 57120847A. Gas sensor e.g. for halogen(s), ammonia, Lewis acid etc. - comprising detector bed contg. phthalocyanine dyes, and electric resistance measuring appts.. G01N027/12.

⑬ 日本国特許庁 (JP)
⑭ 公開特許公報 (A)

⑮ 特許出願公開

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G 01 N 27/12

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6928-2G

⑰ 公開 昭和57年(1982)7月28日

発明の数 1
審査請求 未請求

(全 3 頁)

⑱ ガスセンサ

⑲ 特 願 昭56-6326

⑳ 出 願 昭56(1981)1月21日

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㉔ 代 理 人 弁理士 田辺浦郎

明 細 書

1 発明の名称

ガスセンサ

2 特許請求の範囲

- 1 フタロシアニン顔色素を検知ガス種のセンサベツドとするガス検知部と電気抵抗測定器とより成るガスセンサ。
- 2 センサベツドが真空蒸着法でガラス基板またはプラスチック基板上に形成されたフタロシアニン顔色素の薄膜または圧縮成形法で形成されたフタロシアニン顔色素のペレットである特許請求の範囲第1項記載のガスセンサ。
- 3 検知ガス種がハロゲンガス、ガス状ルイス酸、ガス状のブレンスタッド酸あるいはアンモニアガスである特許請求の範囲第1項記載のガスセンサ。

3 発明の詳細な説明

本発明はフタロシアニン顔色素を検知ガス種のセンサベツドとして用いたガスセンサに関するものである。

従来、この種の装置は、感ガス材料として有機半導体を用いられており、検知対象ガスはメタン、プロパンのような可燃性ガスであり、また高感度化を達成するためにヒーターを用いて構成されていたので、ハロゲンガス、ルイス酸性ガスに対する感度が小さく、かつ構成が複雑

であり、信頼性や保守性に欠ける欠点があつた。

本発明はこれらの欠点を解決するためにヒーターを無くして高感度が達成できる有機半導体を用いたガスセンサであり、かつ検知対象ガスはハロゲンガス、ガス状ルイス酸、ガス状ブレンスタッド酸、あるいはアンモニアガスである。

以下図面について詳細に説明する。

第1図は本発明のガスセンサの検知部の一例の平面図であつて、1はガラス基板、2は真空蒸着により作製したフタロシアニン薄膜、3は金のくし形電極、4は金のリード線、5はカーボン系導電材料である。

これを動作させるにはリード線を通じて、直流電圧を与え、フタロシアニン薄膜にハロゲンガス、ガス状ルイス酸、ガス状ブレンスタッド酸、あるいはアンモニアガスを接触させることにより流れる電流を変化させる。

第2図は第1図のA-A線における縦断面図である。くし形電極、リード線に金を用い、かつ導電材料としてカーボン系を用いた理由はハロゲンガスまたはルイス酸性ガスに対して腐食されないためである。

第3図はガスセンサの回路図であり、6はガス検知部、7は等点調整用可変抵抗器、8は抵抗器、9は直流増幅用集積回路、

10は検流計、11は直流電源である。

これを動作させるにはガスの無い状態で零点調整用可変抵抗器で検流計の出力を零にし、次にガス検知部にガスを触媒させる。ガスの濃度に比例して検流計の針がふれる。ガス濃度特性としてはヨウ素ガスに対して、100 ppmから10000 ppmに検知濃度範囲があり、この時のセンサ抵抗値は1000 K Ω から10 K Ω に変化する。

初期安定性はヒーターを用いるガスセンサにくらべて極めて良く、電圧を印加してすぐに安定する。応答値特性はヨウ素ガス5000 ppmにすばやく挿入した場合のセンサ抵抗値の時間変化は約10秒後に飽和する。また、元の空気中にもどした場合は約30秒で通常の空気中における抵抗値の90%以上に復帰する。

寿命特性として常温常温下では安定であるが、150℃以上の高温になるとフタロシアニオンが蒸発しセンサとしての機能がそこなわれる。

ガスセンサペッドをフタロシアニオンを100 μ g/cm²の圧力で真空圧縮成形してペレットにしてガスセンサを構成した場合も上記の真空蒸着法によるセンサと同等の性能が得られた。

フタロシアニオン色素以外のフタロシアニオン顔料とし

て銅フタロシアニオン、白金フタロシアニオン、ニッケルフタロシアニオン、コバルトフタロシアニオンおよび鉄フタロシアニオンを用いてセンサペッドを構成したガスセンサにおいてもフタロシアニオンと同等の結果を得ることができた。

検知対象ガスとしてはヨウ素ガス以外のハロゲンガスとしてフッ素ガス、塩素ガス、臭素ガスについても試み、検知可能であることを確かめた。ガス状ルイス酸としては五フッ化ヒ素、四フッ化ホウ素、五フッ化リン、五フッ化アンチモンについて、また、ガス状ブレンステッド酸については塩化水素、硫酸ガス、亜硫酸ガス、クロロスルホン酸ガスについてガス検知を試みた結果、ヨウ素ガスと同等の結果を得ることができた。

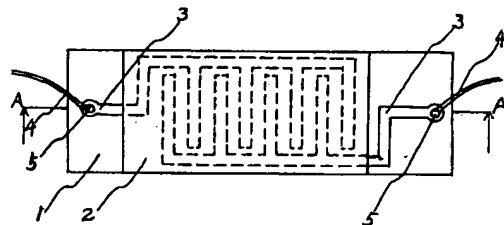
以上説明したように、本発明のガスセンサは人体に有害なハロゲンガス、ガス状ルイス酸、ガス性ブレンステッド酸に対して高感度で安定な検出が可能で、かつ構造が簡単であり安定性も優れていることから、実験で安定性のあるガス検知器、定量分析計として用いられる利点がある。

4 図面の簡単な説明

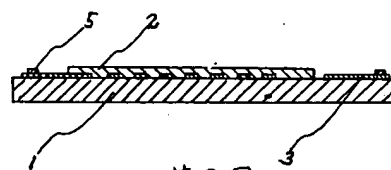
第1図は本発明のガスセンサのガス検知部の一例の平

面図、第2図はその縦断面図、第3図は本発明のガスセンサの回路図である。

- 1 … ガラス基板、2 … フタロシアニオン薄膜、
- 3 … 金のくし形電極、4 … 金のリード線、
- 5 … カーボン系導電塗料、6 … ガス検知部、
- 7 … 零点調整用可変抵抗器、8 … 抵抗器、
- 9 … 直流増幅用集積回路、10 … 検流計、
- 11 … 直流電源



第1図

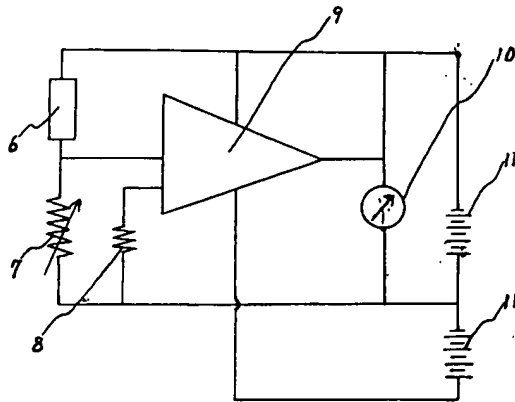


第2図

特許出願人 日本電信電話公社

代理人 弁護士 田辺 浩 郎





第3図

- 132., RU 2085927C. Sensor for concentration of ammonia in liquid and gaseous media - includes cell for sample preparation and measurement cell containing pH-sensitive and comparison electrodes, mixing and gas injection devices. DZHAGATSPANYAN, I E, et al. G01N027/413.



(19) RU (11) 2 085 927 (13) C1

(51) МПК⁶ G 01 N 27/413

РОССИЙСКОЕ АГЕНТСТВО
ПО ПАТЕНТАМ И ТОВАРНЫМ ЗНАКАМ

(12) ОПИСАНИЕ ИЗОБРЕТЕНИЯ К ПАТЕНТУ РОССИЙСКОЙ ФЕДЕРАЦИИ

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применению ионоселективных электродов/ Пер.
с англ. - М.: Мир, 1986, с.21 - 23.

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университет)

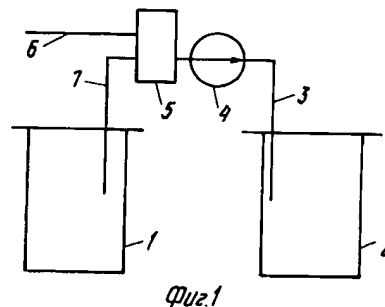
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(54) ДАТЧИК ДЛЯ ОПРЕДЕЛЕНИЯ КОНЦЕНТРАЦИИ АММИАКА В ЖИДКИХ И ГАЗОВЫХ СРЕДАХ

(57) Реферат:

Изобретение относится к измерительной технике, в частности к датчику для определения концентрации аммиака в жидких и газовых средах, содержащему ячейку пробоподготовки и измерительную ячейку с pH-измерительным электродом, электродом сравнения, перемешивающим устройством и узлом подвода пробы, выполненным в виде барботирующего устройства, соединенного с ячейкой пробоподготовки. 2 ил.



RU 2 085 927 C1

RU 2 085 927 C1



(19) **RU** ⁽¹¹⁾ **2 085 927** ⁽¹³⁾ **C1**
 (51) Int. Cl.⁶ **G 01 N 27/413**

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FOR PATENTS AND TRADEMARKS

(12) **ABSTRACT OF INVENTION**

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(46) Date of publication: 27.07.1997

(71) Applicant:
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tehnologicheskij institut (tekhnicheskij universitet)

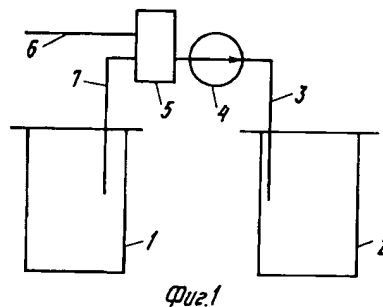
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(54) **TRANSDUCER FOR MEASURING AMMONIA CONCENTRATION IN LIQUID AND GASEOUS MEDIA**

(57) Abstract:

FIELD: measurement technology.
SUBSTANCE: transducer has sample preparation cell and measuring cell with pH measuring electrode, comparison electrode, mixer, and sample feeder in the form of bubbling device connected to sample preparation cell. EFFECT: improved design. 2 dwg



RU 2 085 927 C1

RU 2 085 927 C1

Изобретение относится к измерительной технике и может быть использовано в химических и медико-биологических анализаторах для контроля концентрации аммиака в жидких и газовых средах.

Наиболее близким по сущности к предлагаемому изобретению и выбранным за прототип является датчик аммиака фирмы "Орион" (модель 95-10), принципиальная схема которого приведена в книге ("Справочное руководство по применению ионселективных электродов: Пер. с англ.-М. Мир, 1986, с.21-23).

Этот датчик представляет собой измерительную ячейку, в состав которой входят два электрода (рН-измерительный и электрод сравнения) и узел поступления пробы через газопроницаемую мембрану.

Недостатками прототипа являются:

недостаточная чувствительность (диапазон определения 10^{-6} - 10^{-1} моль/л); высокая инерционность при переходе от измерений в пробах с высокими концентрациями аммиака к измерениям в пробах с низкими время отклика по уровню от 0,95 до 5 мин;

недостоверность определений концентрации аммиака в газовых пробах с низкой влажностью и в водных растворах, содержащих органические вещества.

Задачей, которую решает изобретение, является усовершенствование конструкции датчика для увеличения чувствительности датчика, снижения инерционности и обеспечения достоверности определения концентрации аммиака в газовых средах с различной влажностью и в жидких средах, содержащих органические вещества.

Сущность изобретения сводится к следующему.

Датчик для определения концентрации аммиака в жидких и газовых средах дополнительно содержит барботирующее устройство, соединенное с ячейкой пробоподготовки, и перемешивающее устройство. Электролитом датчика служит микромолярный раствор NH_4Cl .

На фиг.1 изображена блок-схема датчика; на фиг.2. представлена сущность работы измерительной ячейки.

Датчик содержит ячейку пробоподготовки 1 и измерительную ячейку 2. Измерительная ячейка 2 соединена с трубопроводом 3, на котором расположены воздушный насос 4 и кран 5. Кран 5 соединяет трубопровод 3 с трубопроводом 6, сообщающимся с воздухом, и трубопроводом 7, сообщаящимся с ячейкой пробоподготовки 1.

Измерительная ячейка состоит из рН-измерительного электрода 1, электрода сравнения 2, барботирующего устройства 3 и перемешивающего устройства 4.

Принцип работы измерительной ячейки (фиг.2) основан на регистрации изменения рН электролита после растворения в нем аммиака. Аммиак подается через барботирующее устройство 3, расположенное в верхней части измерительной ячейки. Работу перемешивающего и барботирующего устройств обеспечивают интенсивный массообмен аммиака и его быстрое растворение в электролите. Электролит с растворенным аммиаком диффундирует из верхней в нижнюю часть измерительной ячейки, где расположены рН-измерительный

электрод 1 и электрод сравнения 2. Электролитом служит микромолярный водный раствор NH_4Cl . Разность потенциалов между электродами 1 и 2 пропорциональна рН электролита. Изменение рН электролита пропорционально логарифму концентрации аммиака.

Датчик работает следующим образом (фиг.1).

1. Измерение в жидкостях. Жидкая проба помещается в ячейку 1, в которой находится раствор NaOH или KOH с рН не менее 12. Аммиак, содержащийся в пробе в виде ионов аммония (NH_4^+) под действием щелочи переходит в газовую фазу (NH_3) и накапливается в верхней части ячейки 1. Кран 5 переведен в положение, соединяющее трубопровод 3 с трубопроводом 7. Аммиак из ячейки 1 нагнетается воздушным насосом 4 через трубопроводы 7 и 3 в измерительную ячейку 2.

2. Измерение в газах. Газообразный аммиак нагнетается воздушным насосом 4 через трубопроводы 6 и 3 в измерительную ячейку 2. Кран 5 переведен в положение, соединяющее трубопровод 6 с трубопроводом 3.

Газообразный аммиак, барботируясь в верхнюю часть измерительной ячейки, растворяется в электролите. Электролитом служит микромолярный раствор NH_4Cl . Вследствие барботажа и работы перемешивающего устройства скорость растворения аммиака выше скорости диффузии аммиака в неподвижной среде в 10^5 раз. Этим обеспечивается низкая инерционность датчика. Превращения аммиака описываются уравнением Гендерсона-Гассельбаха:

$$\lg(\text{NH}_4^+/\text{NH}_3) = \text{pH} - \text{pK} \quad (1)$$

где NH_4^+ и NH_3 концентрации ионной и газовой форм аммиака, pK - константа диссоциации аммиака, приближенно равная 9. Поскольку рН микромолярного раствора NH_4Cl ниже 9, то по уравнению 1 аммиак в

электролите находится в виде ионов NH_4^+ . Применение в качестве электролита низкомолярного раствора NH_4Cl (10^{-6}) увеличивает чувствительность датчика до 10^{-9} моль/л. Перемешивающее устройство обеспечивает устойчивую работу рН-измерительного электрода и электрода сравнения. Подвод аммиака в измерительную ячейку барботажем, а не с помощью самодиффузии через газопроницаемую мембрану, позволяет достоверно определять концентрацию аммиака и в газах с различной влажностью, и в жидкостях, содержащих органические вещества.

Преимуществами предлагаемого устройства являются:

высокая чувствительность (диапазон определения 10^{-9} - 10^{-1} моль/л);

низкая инерционность (время отклика по уровню 0,95 не более 2 мин на всем диапазоне концентраций);

достоверность определения концентрации аммиака в газовых пробах с различной влажностью и в водных растворах, содержащих органические вещества (например биологических жидкостях).

Формула изобретения:

Датчик для определения концентрации аммиака в жидких и газовых средах, содержащий ячейку пробоподготовки и измерительную ячейку с рН-измерительным электродом, электродом сравнения и узлом

подвода пробы, отличающийся тем, что узел подвода пробы выполнен в виде барботирующего устройства, соединенного с ячейкой пробоподготовки, а внутри измерительной ячейки расположено перемешивающее устройство.

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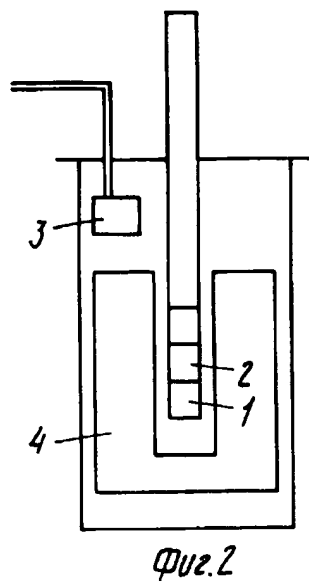
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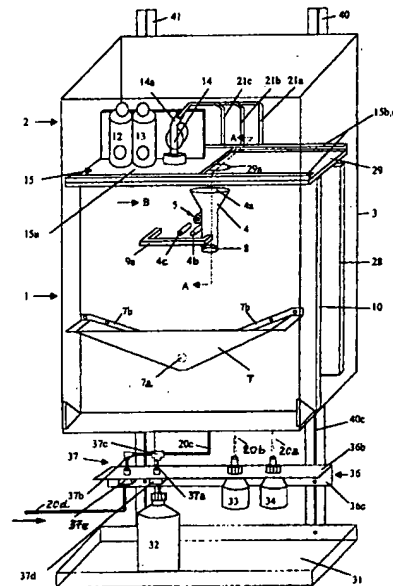
DE 36 05 695 C2
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US 2001/00 44 153 A1;

54 Analysegerät

57 Bei einem bekannten automatisch arbeitenden Analysegerät zur Konzentrationsbestimmung solcher Bestandteile in einer Flüssigkeit, die bei Zusammentreffen mit einer Testsubstanz einen Farbumschlag ergeben, ist für jede Testsubstanz ein getrennter Testbehälter vorgesehen, in den jeweils die Testsubstanz und die zu testende Flüssigkeit eingebracht und der resultierende Farbumschlag photometrisch ausgewertet wird. Durch die Vielzahl der Testbehälter ist der mechanische und elektronische Geräteaufbau kompliziert und teuer. Aufgabe der Erfindung ist die Schaffung eines neuen, einfachen und kostengünstigeren Analysegerätes.

Erfindungsgemäß ist ein einziger Testbehälter (4) sowie ein zentrales Steuergerät (11) zur Steuerung der Testbehälterbefüllung vorgesehen, wobei zur Konzentrationsbestimmung eines ersten Bestandteiles der Testbehälter (4) mit der zu testenden Flüssigkeit und der betreffenden Testsubstanz (33) befüllt und nach photometrischer Farbumschlagsauswertung (9a, 9b) entleert wird. Dann werden zur Konzentrationsbestimmung weiterer Bestandteile die genannten Schritte mit den entsprechenden Testsubstanzen (34) und zu testenden Flüssigkeiten in analoger Weise wiederholt.

Das Analysegerät dient speziell zur Konzentrationsbestimmung von schädlichen Bestandteilen in Fischzuchtteichen oder Kläranlagen.



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昭和50年9月25日

特許庁長官 殿

発 明 の 名 称 アンモニアの連続分析法およびその装置
特許請求の範囲に記載された発明の数(2)

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50 114666

明 細 書

発 明 の 名 称 アンモニアの連続分析法およびその装置

特 許 請 求 の 範 囲

1. 試料ガス中に既知濃度の窒素酸化物を一定量添加した後、アンモニアを窒素酸化物によつて窒素まで還元し得る触媒層を通過させ、試料ガス、窒素酸化物添加後の試料ガスおよび触媒層通過後の試料ガスの3種のガス中の窒素酸化物の濃度を窒素酸化物分析計で計測し、その3種の値をアンモニア濃度に換算することを特徴とするアンモニア分析法。

2. アンモニアを含む試料ガス中に、窒素酸化物標準ガスを一定量添加するための系統、前記NO標準ガスを添加した後の試料ガスを通じて窒素酸化物によりアンモニアを酸化するための触媒を充填した反応器、試料ガス、窒素酸化物添加後の試料ガスそして反応器を通過してアンモニア酸化反応の終了した試料ガスの3種のガスを、同時に3台のまたは切換えにより順次一

(1)

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台の窒素酸化物分析計に導く装置、さらに窒素酸化物分析計の電気出力をアナログまたはデジタル演算回路によつてアンモニア濃度に比例した電気出力に変換する装置を有することを特徴とするアンモニア連続分析装置。

発 明 の 詳 細 な 説 明

本発明はアンモニアの連続分析方法ならびに装置に係る。特に各種排ガス中の窒素酸化物をアンモニアにより接触還元した後のガスに含まれるアンモニアを正確、高感度かつ迅速に連続分析する方法ならびに装置に関する。

近年大気汚染が進行するに伴って汚染物質の1つである窒素酸化物(以下NO_xと略す)の排出抑制が望まれており、各種排ガス中のNO_xの除去技術の開発が進められている。これら技術の一つである乾式法のなかではNO_xをアンモニアによつて接触還元する方法(以下アンモニア還元法と略す)が工業化可能とされている。

NO_xのアンモニア(以下NH₃と略す)還元法において最も問題となるのはNO_x除去反応塔

(2)

の出口側に流出してくる未反応アンモニアである。これは、イオウ酸化物と反応してアンモニウム塩を生成するのみでなく、大気中に放出されて二次公害を起す可能性があり、特に後者の可能性はLNGだき、ボイラのNO_x除去装置において強い。このため、NO_xのNH₃還元法においては注入するアンモニアの量と流出するNH₃の量は厳密に制御されねばならない。

従来アンモニアの分析は、日本工業規格に規定されている。(1)中和滴定法、(2)インドフェノール法、(3)ネスラー法、(4)溶液電導率法、(5)赤外線ガス分析法、(6)検知管法があるが、(1)は塩基性および酸性ガスの影響があり、また、NH₃濃度100ppm以下には向かない。(2)、(3)は吸取操作発色操作を含め1〜2時間を要する。(4)は電導率を変化させる共存ガスがある場合には使用出来ない。(5)は感度が低く低濃度分析は出来ない。(6)はNH₃濃度の概略しか知れない等々の問題を有している。このため、前述の排ガス中のNO_x除去を目的とするNH₃還元法におけるNH₃濃度の連続分析

(3)

ことを確認した。また、NOとNO₂が共存する場合でも、NOがNO₂より多ければNO_x(NO+NO₂)とNH₃が1モル対1モルに反応しNOとNH₃が1モル対1モルに反応するのと同様である。

さらに上記のNOとNH₃の1モル対1モルの反応は、鉄、バナジウム、タンタム等の遷移金属酸化物を主成分とする触媒表面では非常に大きな反応速度を有し、空間速度0〜100000h⁻¹の間で定量的に進行することを確認している。

このようにNO(もしくはNO₂)とNH₃の反応は、NH₃1モルに対しNO1モルと反応しその反応は空間速度0〜100000h⁻¹の間であれば反応は定量的に進行するため、NOがNH₃より過剰に存在する場合は、NOの減少量がNH₃濃度に等しいことになる。本発明はこの点を基本原理として構成されるNH₃連続分析計である。

以下本発明を図によつて詳細に説明する。

第1図は本発明の一実施例を示すアンモニア連

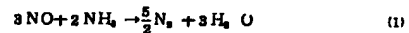
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続分析計である。アンモニアを含んだ試料ガスはリボンヒータ1で保温された試料ガス導入管5通に導入されるが、以下の順に各種の操作が行なわれる。

本発明は、上記の要求に答えて各種排ガスのアンモニア還元脱硝装置におけるNH₃濃度分析に適する高感度かつ共存ガスの影響を受けないNH₃連続分析方法ならびに装置を提供せんとするものである。

本発明の特徴とするところは、NH₃とNO_xを含むガスをNH₃をNO_xにより酸化する活性を有する触媒に接触反応させ、その前後のNO_x量を測定しNO_xの変化をNH₃濃度に変換する点、また、高感度NO_xメータを使用して低濃度NH₃分析を可能とした点にある。

一般にNH₃とNOの反応は(1)式で示されるようにNH₃2モルに対しNO3モルが



反応するとされてきた。しかしながら本発明者等は金属酸化物を主成分とする触媒上でのNOとNH₃との反応を詳細に検討した結果、酸素供下ではNH₃1モルに対しNO1モルが反応する

(4)

反応するとされてきた。しかしながら本発明者等は金属酸化物を主成分とする触媒上でのNOとNH₃との反応を詳細に検討した結果、酸素供下ではNH₃1モルに対しNO1モルが反応する

(1) 試料ガスの1部は、冷却器6aで冷却され凝縮した水を水トラップ7aで除去された後ニードルバルブ8a、ポンプ9aを経て窒素酸化物分析計(以下NO_xメータ)11aに導かれてNO_xが測定される。

(2) 残った試料ガス中に窒素酸化物標準ガス(本例ではNOスパンガス)がNOスパンガスポンベ10からニードルバルブ8bを通して一定量添加され、NH₃とNO_xの反応の等量以上のNO_x濃度とされる。

(3) NOスパンガス添加後の試料ガスの一部は、冷却器6b、水トラップ7b、ニードルバルブ8c、ポンプ9bを経てNO_xメータ11bでガス中のNO_xが測定される。

(4) (1)〜(3)までの操作を受けて残った試料ガスは電気炉2によつて加熱された反応管3に導かれ

(6)

反応管3中に充填された触媒4によつて反応が完結させられる。その後、冷却器6c水トラップ7cニードルバルブ8d、ポンプ9cを経てNO_xメータ11cで反応後に残存するNO_xが測定される。

仮に試料ガス中にNH₃とNOの両者が存在する場合を考える。ここで、

試料ガス中のNO濃度をC_{NO}^a。(NOxメータ11aで測定される)

NOスパンが注入後のNO濃度をC_{NO}^b。(NOxメータ11bで測定される)

触媒層通過後の試料ガス中のNO濃度をC_{NO}^c。(NOxメータ11cで測定される)

あらかじめ測定されているNOスパンガスのNO濃度C_{NO}^d。

とするならば、NH₃とNOが定量的に1モル対1モルに反応するので試料ガス中のNH₃濃度C_{NH3}は(9)式によつて示される。

$$C_{NH_3} = \frac{C_{NO}^d - C_{NO}^a}{C_{NO}^d - C_{NO}^b} \times (C_{NO}^b - C_{NO}^c) \quad (9)$$

(10)

可変電圧13で与えられるNOスパンガスに比例する電圧とを演算回路12に導き、先に示した(7)式の演算を行なわせ、NH₃濃度C_{NH3}に比例した出力電圧を得るようにしてある。演算回路12の出力は記録計14に導かれ連続的に記録される。本発明による分析原理ならびに装置は以上に説明した如くであるが、さらにつけ加えておく点として、(1)~(5)までがある。

(1) NO_xメータは再現性のあるものならばなんでもよいが応答の早いNO_xメータ(たとえばケミルミネツセンス方式)が適する。

(2) 触媒は、NOとNH₃との反応に触媒作用するものであれば何でもよいが下記の注意を必要とする。

(1) NH₃とNOの反応比率を決定しておく必要がある。

(2) NH₃とNOの反応が定量的に反応する条件を適定しておく必要がある。

(3) 試料ガス中にNH₃とNOとNO_xが存在する場合NOスパンガス注入後、NOがNO_x。

(11)

また、NOxメータ11a, 11b, 11cで出力される電圧を各V_{NO}^a, V_{NO}^b, V_{NO}^cと記号で示すならば、(3)~(5)式の関係がある。

$$V_{NO}^a = \alpha_1 C_{NO}^a \quad (3)$$

$$V_{NO}^b = \alpha_2 C_{NO}^b \quad (4)$$

$$V_{NO}^c = \alpha_3 C_{NO}^c \quad (5)$$

ここでα₁, α₂, α₃は比例定数

あらかじめNO_xメータ11a, 11b, 11cを校正によりα₁=α₂=α₃なるようにしておき、NOスパンガスに比例する電圧が(6)式で

$$V_{NO}^d = \alpha_1 C_{NO}^d \quad (6)$$

で与えられるならば

$$\frac{V_{NO}^d - V_{NO}^a}{V_{NO}^d - V_{NO}^b} \times (V_{NO}^b - V_{NO}^c) = \alpha_1 C_{NH_3} \quad (7)$$

(2)~(6)式より、(7)式が導かれ、NH₃濃度

C_{NH3}に比例する電気出力が得られる式が導かれる。

従つて本発明では第1図にあらかじめ同一のNOスパンガスで校正され、α₁=α₂=α₃とされたNO_xメータ11a, 11b, 11cの出力電圧と

(8)

より多ければ、NH₃とNOは1モル対1モルに反応するがNO_xが多い場合には反応比率が変化するのでNOがNO_xより多くなるように注意する必要がある。

(4) NH₃とNOが1モル対1モルで反応するためには酸素がNO濃度の4倍以上必要であるので、試料ガス中に酸素を含有しない場合等には試料ガス中に酸素と添加するかもしくはNOスパンガス中に酸素を含有させておく必要がある。

(5) NH₃とNOの反応に選択的な触媒作用を有する触媒を用いることによりSO₂, SO₃, CO, CCl₄, H₂O, N₂等の共存ガスの影響は受けない。次に図2に示すのは、他の実施例を示すNH₃。

連続分析計である。

第2図において、リボンヒータ1~NOスパンガスポンプ10までの各部の機能については、第1図と同様であるが、第2図と異なり第2図中のNO_xメータ11a, 11b, 11cで測定されたNO_x濃度C_{NO}^a, C_{NO}^b, C_{NO}^cに相当する値は、第2図中のガス切換装置15によつて順次切換えられてNO_xメ

ータ17に導かれ順次測定される。

即ち、ポンプ9a, 9b, 9cによつて送られてくる3種のガスはコントロール部16によつて制御されたガス切換装置15によつて順次NO_xメータ17に導かれNO_x濃度が測定される。このとき3種のガスのうちNO_xメータに送られているガスをのぞく2種のガスは大気中に放出される。従つて、NO_xメータの出力電圧は、順次一定間隔で切換えられるガス中のNO濃度に比例しており、 $V_{NO}^a \rightarrow V_{NO}^b \rightarrow V_{NO}^c \rightarrow V_{NO}^d \rightarrow V_{NO}^e \dots$ という変化を示す。

NO_xメータの電気出力は常時A-Dコンバータ(アナログ-デジタルコンバータ)18によつて、デジタルな値に変換された後、マルチプレクサ-19によつて記憶装置20a, 20b, 20cのいずれかに送られ記憶される。即ち、ガス切換装置15がポンプ9aからのガスをNO_xメータ17に送つてゐる場合にはNO_xメータ17、電気出力及びD-Aコンバータ18の出力は、NO濃度C_{NO}に比例しており、マルチプレク

サ-19によつて

24によつて連続的に記録される。ガス切換装置15以後の各部のタイムチャートを第1図に示した装置に対する注意事項は第2図に示した装置におけるものと同様であるが、第2図の装置における特徴を示せば

- (1) NO_xメータが1台でよい
- (2) NO_xメータが3台の場合に生じる調整による誤差が生じない
- (3) 切換によるため応答が遅くなるが応答の速い(ケミルミネツセンスタイプなど)NO_xメータを使用することにより各部のNO_xの測定を1分以内にすることが出来るため、実用上は問題ない。

などがある。

以上第1図、第2図によつて本発明の原理及び装置の説明を行なつた。本発明によるNH₃分析上得られる利点は下記の如くである。

- (1) 連続分析できる
- (2) NO_xメータに高感度で応答の速いものを使用すれば高感度で応答速度の大きいNH₃分析

サ-19によつて、記憶装置20aに送られ記憶される。同様にポンプ9bからのガスの場合には記憶装置20b、ポンプ9cからのガスの場合には、記憶装置20cに記憶されることになる。コントロール部16によつてガス切換装置15、マルチプレクサ-19、記憶装置20a, 20b, 20cは同期して制御されており、記憶装置20a, 20b, 20cに記憶された内容を $V_{NO}^a, V_{NO}^b, V_{NO}^c$ とするならば、 $V_{NO}^a \leftrightarrow V_{NO}^b, V_{NO}^b \leftrightarrow V_{NO}^c, V_{NO}^c \leftrightarrow V_{NO}^a$ と常に $V_{NO}^a, V_{NO}^b, V_{NO}^c$ に対応している。

かように記憶された $V_{NO}^a, V_{NO}^b, V_{NO}^c$ の3種のデジタルな値とデジタルスイッチ21によつて与えられる V_{NH}^d に相当するデジタル値 V_{NH}^e とはデジタル演算回路22に送られ、(7)式に相当する演算がデジタル処理によつて行なわれる。演算回路22の出力であるNH₃濃度C_{NH}に比例したデジタル値は次にくるD-Aコンバータ(デジタル-アナログコンバータ)23によつてアナログ値に変換されたのち記録計

に

計が得られ、低濃度のNH₃分析ができる。

- (3) SO₂, CO₂, CO, H₂O等共存ガスの影響を受けない。
- (4) 流量測定が必要がない。

以下に実施例を示す。

実施例1

第1図に示したNH₃連続分析装置を用いて重油ボイラ排ガス中に含まれるNH₃濃度を測定した。排ガスの組成は下記の如くである。

NO _x	150~170 ppm
SO _x	600~700 ppm
SU _x	50~60 ppm
O ₂	3~6%
H ₂ O	8~11%
CO ₂	11~14%
N ₂	残り

上記組成の排ガス中にNH₃添加量を変化させて添加し、本発明によるNH₃連続分析装置による分析値とインドフェノール法による分析値の比較を行なつた。

本実施例における分析装置各部の仕様は

反応管径 10^{mm}

触媒 : TiO_2 , MO_3 , V_2O_5 の酸化分
焼結体の 10~20メッシュの粒
状物

炉内温度 : 380℃

各 NO_x ノータへ導くガス量 : 0.5 L/min

触媒に対する空間速度 : 20000 h⁻¹

である。

第3図にインドフェノール法と本発明による NH_3 濃度の分析の比較結果を示した。第3図は本発明の分析装置による値とインドフェノール法の分析値がよく一致していることを示している。インドフェノール法の場合はガスサンプリングから分析終了まで2時間を必要としたのに対し本分析装置は、常時連続的に NH_3 濃度の変化を記録出来た。

実施例2

第2図に示した NH_3 連続分析計を用いてLNG 燃焼ガス中に添加した NH_3 濃度の分析を行ない

(15)

値と本分析装置の値とはよく一致しており、このことから本分析装置が低濃度でもきわめて安定した分析が可能であることを示している。

図面の簡単な説明

第1図は本発明の一実施例を示すアンモニア連続分析装置の系統図、第2図も本発明の他の実施例を示すアンモニア連続分析装置の系統図である。第3図は第1図に示したアンモニア連続分析装置を使用した重油燃焼ガス中の NH_3 濃度の分析値とインドフェノール法による分析値との比較を示したグラフ、第4図は第2図に示したアンモニア連続分析装置を使用したLNG燃焼ガス中の NH_3 濃度の分析値とインドフェノール法による分析値との比較を示したグラフである。

符号の説明

- | | |
|---|---------|
| 1 | リボンヒータ |
| 2 | 電熱炉 |
| 3 | 反応管 |
| 4 | 触媒 |
| 5 | 試料ガス導入管 |

その値とインドフェノール法による分析値の比較を行なった。

分析計に使用した触媒ガス流量温度は第1図と同様である。以下にLNG燃焼ガスのガス組成を示す。

NO_x	40~50 ppm
CO	10~11%
H_2O	15~16%
O_2	2~3%
N_2	残り

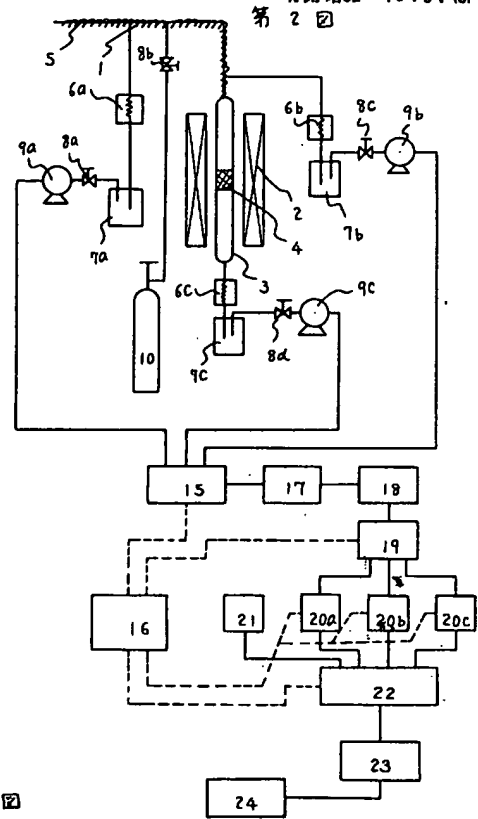
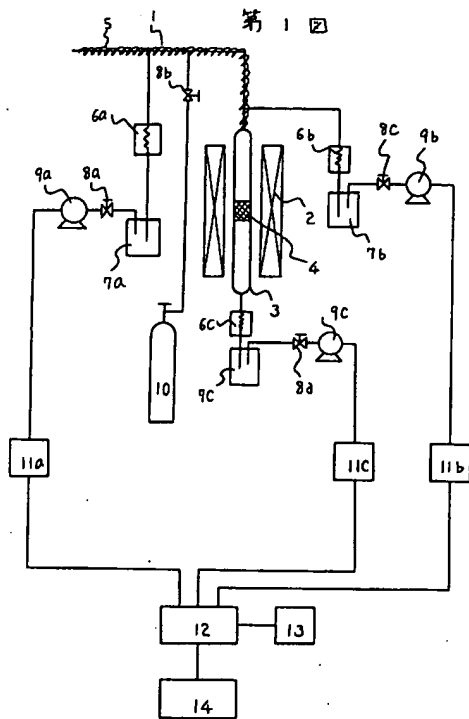
第4図に本発明による NH_3 分析装置の分析値とインドフェノール法による分析値の比較を行なった結果を示した。第4図には、本分析装置が一定の指示値を示している場合に行なったインドフェノール法による分析値の値が何点か示してある。本分析装置の指示値が一定値を示している場合でもインドフェノール法による分析値はバラツキているが、これは NH_3 が低濃度によるための誤差がインドフェノールの場合に大きいことを示している。バラツいているインドフェノール法の分析

(16)

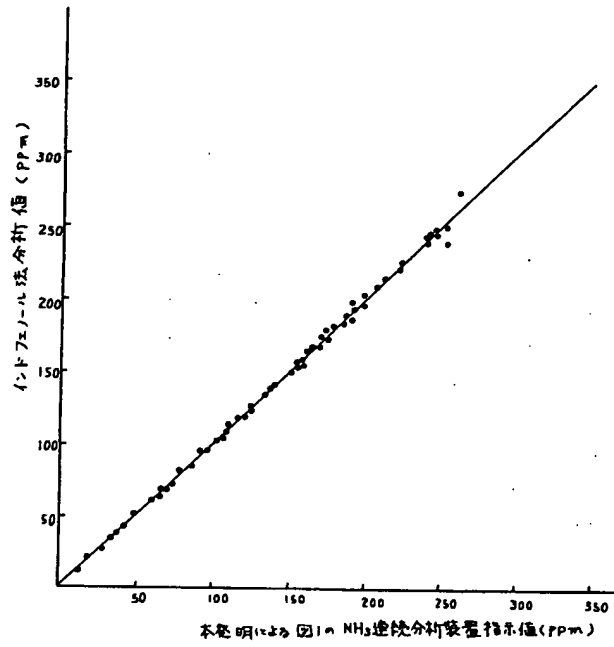
6a~6c	冷却器
7a~7c	水トラップ
8a~8d	ニードル弁
9a~9c	ポンプ
10	NO標準ポンプ
11a~11c	窒素酸化物分析計

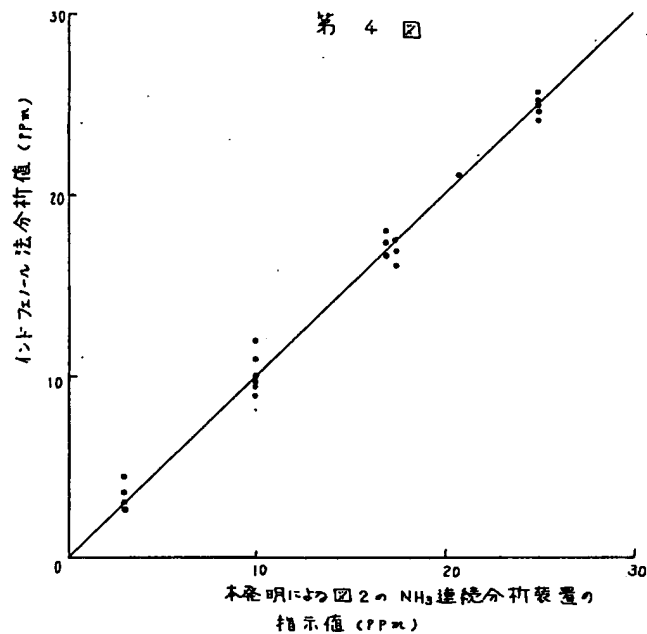
代理人 弁理士 高橋明夫





第 3 図





添附書類の目録

- (1) 明 細 書 1通
- (2) 図 面 1通
- (3) 要 件 状 1通
- (4) 特 許 願 本 1通

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3/34

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C-6923-4D

審査請求 未請求 発明の数 1 (全6頁)

⑮ 発明の名称 生物学的アンモニア濃度測定装置

⑯ 特 願 昭59-222243

⑰ 出 願 昭59(1984)10月24日

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明 細 書

1. 発明の名称

生物学的アンモニア濃度測定装置

2. 特許請求の範囲

(1) 廃水を生物学的に処理する活性汚泥処理工程における活性汚泥の一部を一定量導入された小型曝気槽と、前記小型曝気槽内の活性汚泥の酸素消費速度を測定する手段と、前記小型曝気槽内に硝化抑制剤を注入する手段と、硝化抑制剤を前記小型曝気槽内に注入しない場合と注入した場合の酸素消費量の差を積分値として求める演算部とを備え、この積分値によりアンモニア濃度を測定することを特徴とする生物学的硝化速度測定装置。

(2) 特許請求の範囲第1項に記載の生物学的アンモニア濃度測定装置において、二槽の小型曝気槽と、曝気槽ガスより酸素消費速度を測定する手段を備え、一方の小型曝気槽で硝化抑制剤を注入しない場合の酸素消費量を測定するとともに他方の小型曝気槽で硝化抑制剤を注入した場合の酸素消費量を測定し、両者の差の積分値を演算部によ

り求めることによりアンモニア濃度を測定するようにした生物学的アンモニア濃度測定装置。

3. 発明の詳細な説明

(発明の属する技術分野)

本発明は廃水の生物学的処理に際して、硝化プロセスにおける曝気槽内のアンモニア濃度を曝気槽ガスより測定する生物学的アンモニア濃度測定装置に関する。

(従来技術とその問題点)

環境汚染の進行に伴い、廃水中の栄養塩類、とりわけ窒素およびリン化合物に起因する河川、湖沼、あるいは海域の富栄養化現象が深刻な社会問題となっている。この富栄養化の防止策として廃水中の窒素あるいはリン化合物の除去技術が開発されている。このうち、窒素除去法としては、生物学的脱窒法が最も有望とされている。この方法は好気性条件下において活性汚泥とともに生育する硝化菌によりアンモニアを亜硝酸あるいは硝酸に酸化する硝化プロセスと、嫌気性条件下において通性嫌気性菌が亜硝酸あるいは硝酸イオンの酸素

を吸収に利用することにより亜硝酸あるいは硝酸イオンを窒素ガスに変換する脱硝プロセスとからなる。これら両プロセスの組合せにより排水中の窒素化合物は最終的に窒素ガスとして除去される。

しかし、前述の硝化プロセスは硝化菌の増殖速度が遅く、また、水温などの影響を受けやすいことからその管理が難しく、したがって生物学的脱窒法を適用化する上で硝化プロセスの適正な管理が最大の課題の一つである。

硝化プロセスを管理するためには硝化槽内のアンモニア濃度を測定し、アンモニアが確実に硝化されているかをチェックする必要がある。このためには、アンモニアイオンの分析用として開発された選択性電極を使うことが考えられた。しかし、イオン選択性電極は安定性に乏しく、オンライン計器としての使用には必ずしも充分とはいえない。

そこで、本発明者は先に排水中の有機窒素とアンモニア性窒素を脱気脱ガス測定にてオンライン測定する方法を開発し、特許出願中である。

(特開昭53-25113号)。この方法は第3図に示

されるように前曝気槽1、固定床もつ主曝気槽2、後曝気槽3、酸素分析計4、二酸化炭素分析計5、調整器6、排水サンプリングポンプ7、空気ポンプ8、定量バルブ9で構成された装置を用い、前曝気槽1で排水中の酸素と二酸化炭素を大気中のそれぞれの分圧に対する平衡濃度にし、次いで主曝気槽2において固定に付着されている活性汚泥の作用により80%程度の酸化と窒素成分の硝化を行い、最後に後曝気槽3で排水中の酸素および二酸化炭素を再び大気中のそれぞれの分圧に対する平衡濃度にして放出する。このときの主曝気槽2と後曝気槽3で得られる酸素消費量と二酸化炭素発生量の差より排水中の有機窒素およびアンモニア性窒素を求めるものである。

すなわち、この方法は電極法とは異なり、放出端が下水と直接接触することがないため、放出端のよごれから来る放出端部の低下がなく、安定したオンライン測定が望まれる。

ところが、前述の公知方法には次の欠点が存在することが明らかになった。

(1) 二酸化炭素は水中に多く溶解するため、二酸化炭素生成量を測定するためには前曝気と後曝気を行って排水および流出水に含まれる二酸化炭素の影響を除去する必要がある。しかし、排水として曝気槽内の活性汚泥をサンプリングすると、活性汚泥中の硝化菌の作用により前曝気中に硝化反応が進み、アンモニア濃度の測定値が低くなる傾向にあった。

(2) 測定に際して酸素分析計と二酸化炭素分析計が用いられるが、これらはそれぞれ、測定原理が異なるため、これら分析計間の相対誤差がアンモニア濃度の小さい場合には測定誤差として大きく現れていた。

これらの欠点はアンモニア濃度の測定に当たり、二酸化炭素の生成速度を測定することに起因している。

(発明の目的)

本発明の目的は生物学的脱窒法における硝化プロセスを適正に管理するためのアンモニア濃度測定の必要性に鑑みて、従来技術では固定が困難で

あったアンモニア濃度の低い場合でも曝気槽内のアンモニア濃度をオンラインで安定して測定できる生物学的アンモニア濃度測定装置を提供することにある。

(発明の要旨)

前述の目的を達成するため、本発明によれば、排水を生物学的に処理する活性汚泥処理工程における活性汚泥の一部を一定量導入された小型曝気槽と、この槽内の活性汚泥の酸素消費速度を測定する手段と、この槽内に硝化抑制剤を注入する手段と、硝化抑制剤を前記小型曝気槽内に注入しない場合と注入した場合の酸素消費量の差を微分値として求める演算器とを備え、この微分値によりアンモニア濃度を測定することを特徴とする。

(発明の実施例)

以下、本発明装置を具体的に説明する。

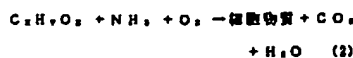
まず、本発明にかかる曝気脱ガスによる生物学的アンモニア濃度測定装置の原理を詳述すると次のとおりである。

一般に、排水を活性汚泥法により処理すると、

800 成分が酸化除去されると同時に廃水中のア
ンモニア成分が亜硝酸あるいは硝酸に酸化される、
いわゆる硝化作用が現れる。これは活性汚泥中に
生育する硝化菌によるものである。硝化菌にはア
ンモニアを亜硝酸に酸化するNitrosomonasと亜硝
酸を硝酸に酸化するNitrobacterがある。これら
硝化菌は独立栄養性細菌と呼ばれ、二酸化炭素、
すなわち、水中の炭酸塩を唯一の炭素源として増
殖する。これは廃水中の有機物を炭素源として増
殖する800 酸化菌(従属栄養性細菌)と大きく異
なる点である。また、800 酸化菌および硝化菌は
ともに好気性細菌であるが、800 酸化菌は廃水
中の有機物を水と二酸化炭素に酸化する際のエネ
ルギーを増殖に利用するのに対し、硝化菌はアン
モニアを亜硝酸に、あるいは亜硝酸を硝酸に酸化
する際のエネルギーによって増殖する。曝気槽内
ではこれらの酸化反応と微生物の増殖が行われる
が、それぞれの化学量論式は以下のとおりである。

まず、800 酸化菌については、有機物の酸化、
細胞物質の合成、細胞物質の酸化についてそれぞ

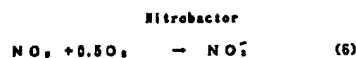
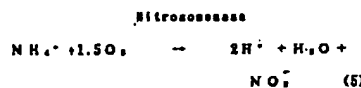
れ式(1)、(2)、および(3)が成り立つ。



また、廃水中の有機性窒素Org-Nは活性汚泥
で処理するとアンモニアになることが知られてお
り、これは式(4)で表される。



次に、硝化菌によるアンモニアおよび亜硝酸の
酸化反応は、



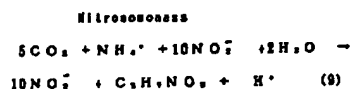
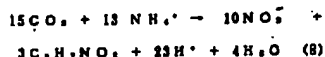
となり、全体で



となる。

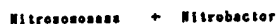
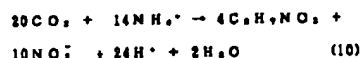
硝化菌はこれらの酸化反応のエネルギーを利用

して増殖するが、その増殖式はNitrosomonas、
Nitrobacterの實驗式を $C_2H_4NO_2$ と仮定す
ると、それぞれ式(8)および(9)で表される。



(Nitrobacter)

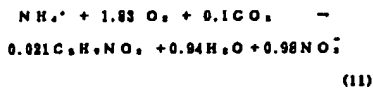
全体として



となる。

一方、硝化菌の生産係数は實驗的に求められて
おり、アンモニア1gの酸化に対し、0.04乃至0.13
gのNitrosomonasが生産され、亜硝酸1gの酸化
に対し、0.02乃至0.07gのNitrobacterが生産さ
れる。これらの値は酸化反応(5)、(6)および(7)
に対して増殖反応(8)、(9)および(10)の割合が

非常に少ないことを示しており、これらの生産係
数を考慮して式(7)と(10)を組み合わせると、酸
化と増殖の全体反応として式(11)が得られる。



ところで、通常の生物学的硝化プロセスではア
ンモニアの亜硝酸への酸化が律速段階となるため
に、アンモニアはほとんど硝酸まで酸化されると
考えてよく、したがって以下の議論は式(11)を用
いて行う。

このように活性汚泥法では、800 酸化菌による
800 成分の除去と、硝化菌によるアンモニアの硝
酸、亜硝酸への硝化が同時に行われるため、その
際に消費される酸素量も両者の反応の合計量であ
る。この反応をバッチ槽で行ったときの関係を第
2図に示す。第2図において、実験Aが實驗され
る酸素消費速度であって、反応開始時点は酸化と
硝化が併わかった酸素消費速度を示すが、活性汚
泥に含まれるアンモニアの硝化が終了した時点で

急激に酸素消費速度が小さくなり、800 酸化圈のみによる酸素消費速度となる。一方、点線Bは800 酸化圈のみによる酸素消費速度で、実験Aと点線Bで囲まれた斜線部分が活性汚泥中に含まれるアンモニアの酸化によって消費される酸素の量である。よって、この酸素消費量が求められれば、(11)式の関係からアンモニア濃度を求めることができる。

ところが、800 酸化圈のみの酸素消費速度を算出することができないため、従来は800 酸化圈による酸素消費速度とはほぼ等しい二酸化炭素生成速度を用いてこの酸素消費速度を測定した。

このため、従来法ではアンモニア濃度測定のために、二酸化炭素生成速度を測定する必要があり、前述のような欠点を有していた。

そこで、本発明者らは酸素消費速度のみをもってアンモニア濃度を測定する方法を鋭意研究の結果、硝化抑制剤を用いることにより800 酸化圈のみによる酸素消費速度が求められることに着目した。ここで硝化抑制剤は800 酸化圈に影響を与え

ずに硝化作用を完全に抑制する必要がある、本発明者らの実験検討の結果、硝化抑制剤としてアリルチオ尿素(以下A.T.U.と略略する)を活性汚泥に対して0.35乃至0.7 mg/g-15 用いれば、本発明の使用目的に達することを明らかにした。よって、このA.T.U.を用いることにより、酸素消費量の測定のみでアンモニア濃度を測定することが可能となった。

以下、本発明を実施例を用いてさらに詳述する。

実施例

第1図は本発明にかかる装置の一具体例の構成図であって、二槽の小型曝気槽、ならびに曝気槽ガスより酸素消費速度を測定する手段を備えた例を示す。10は廃水を生物学的に処理する活性汚泥処理工程における曝気槽であって、この曝気槽10から活性汚泥の一部が原水供給装置11(原水タンク・ブリンダ装置)により、硝化抑制剤添加型の小型曝気槽12および硝化抑制剤添加型の小型曝気槽13に同量ずつ供給される。これらの小型曝気槽12、13は硝化抑制剤添加型の小型曝気槽13が硝化抑制

剤供給装置19を備える以外は全く同じである。

次に硝化抑制剤添加型の小型曝気槽13には硝化抑制剤供給装置18から硝化抑制剤が供給される。さらにこれら二槽の小型曝気槽12、13にはそれぞれ、一定量の空気が空気ポンプ16より定量バルブ17、17を通過して供給され、そして脱泡ベラ15、15の働きでそれぞれ小型曝気槽12、13内の活性汚泥に空気が供給される。その曝気槽ガスは切換バルブ20により一定時間毎に交互に切換られ、曝気槽ガスより酸素消費速度を測定する手段としての酸素分析計21で酸素消費速度が測定され、さらに換算器22で両槽12、13の酸素消費速度の差を求めることにより硝化速度が測定される。第1図中、14、14はそれぞれ脱泡モータ18、18はそれぞれ排水バルブ、23、23はそれぞれPI制御装置である。

ここで小型曝気槽12、13から測定される酸素消費速度は第2図によって説明される。すなわち実験Aは小型曝気槽12で測定される酸素消費速度の経時変化で、実験Bは硝化抑制剤添加型の小型曝気槽13から測定される酸素消費速度の経時変化で

ある。またこの両曝気槽12、13はPI制御装置23、23により常にPI値が等しくなるように制御されるため、800 圈の働きも等しく、よって800 圈による酸素消費量は両槽とも等しい。このため、換算器22で両槽からの酸素消費速度の差を積分し(11)式の関係を用いて換算することにより試料に含まれるアンモニア濃度を求めることができる。

(発明の効果)

以上のように、本発明によれば、曝気槽内のアンモニア濃度を、曝気槽ガス中の酸素分析のみによって測定しうるため、安定して正確なオンライン測定が可能である。また、構成分析装置としては、従来法では必要とされていた二酸化炭素分析計を必要としなくなったから、非常に安価になるとともに分析装置間の相対誤差が解消され、分析計の調整作業も単純した。

4. 図面の簡単な説明

第1図は本発明にかかる測定装置の一具体例の構成図を示し、第2図は本発明にかかる測定装置の原理の説明したグラフを示し、第3図は従来の

固定装置の構成図を示す。

10 . . . 曝氣槽、 12、13 . . . 小型曝氣槽、

19. . . 硝化抑制剂供給装置、21. . . 酸素

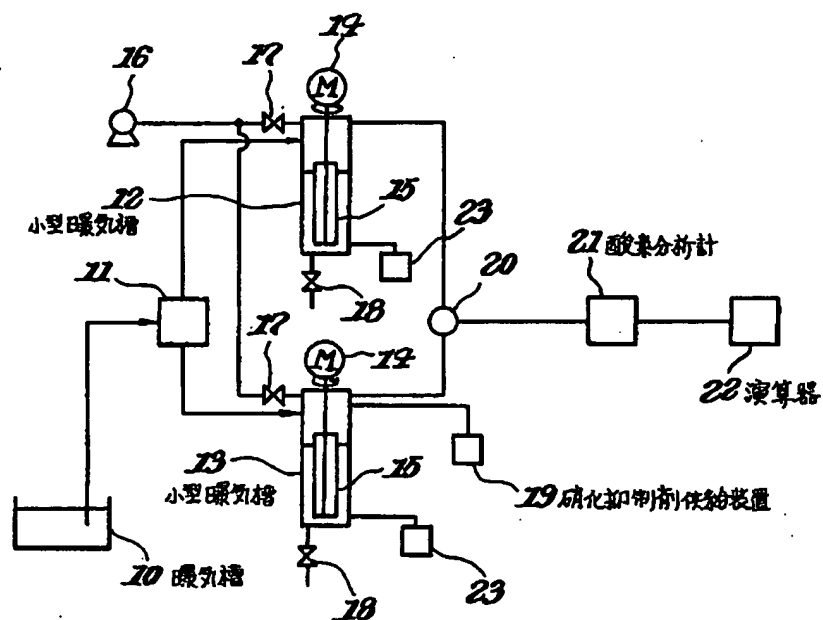
分析計、 22 . . . 演算題

特許出願人 富士電機株式会社

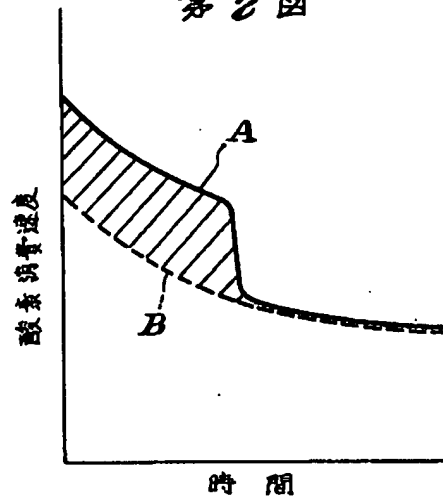
代 理 人 奔 理 士 驗 容



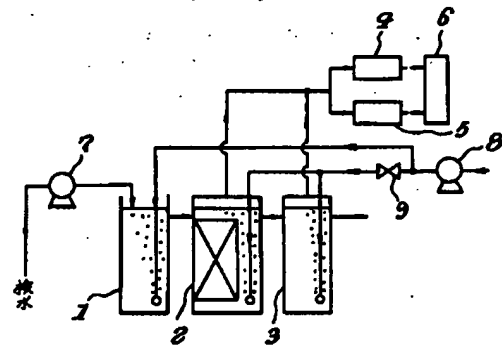
第 1 圖



第2圖



第3圖



⑩ 日本国特許庁(JP)

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⑮ 発明の名称 アンモニアガス測定装置

⑯ 特 願 昭63-274233

⑰ 出 願 昭63(1988)10月29日

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明 細 書

1. 発明の名称

アンモニアガス測定装置

2. 特許請求の範囲

(1) 測定ガスを導く第1のガス系統と、還元触媒を有し、測定ガス中の窒素酸化物とアンモニアを反応させる第2のガス系統と、窒素酸化物検出器と、第1のガス系統と第2のガス系統を切り替えて前記窒素酸化物検出器に接続する切替え手段と、前記切替え手段の動作を制御する制御部とを備え、前記制御部は、前記窒素酸化物検出器の出力を取り込んでアンモニア濃度を算出する演算部と、アンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの少なくとも1個の大きさが大きくなると前記切替え手段の切替え周期を短かくするように前記切替え手段の切替え周期を決定する切替え制御部とを備えているアンモニアガス測定装置。

3. 発明の詳細な説明

(産業上の利用分野)

本発明はアンモニアと窒素酸化物を含むガス中の少なくともアンモニア濃度を測定する装置に関するものである。

アンモニアガス測定装置は、例えば煙道排ガス脱硝装置において脱硝の程度と残留アンモニアガスを監視するために利用することができる。

(従来の技術)

煙道排ガスなどには窒素酸化物が含まれるので、アンモニアで窒素酸化物を還元して窒素酸化物を除去する脱硝装置が用いられる。

アンモニアガスも有害ガスであり、脱硝装置から大気中に排出される残留アンモニアガスは二次公害を引き起こすので、アンモニアガス添加量を制御するために脱硝装置の出口における残留アンモニアガスを監視する必要がある。

アンモニアガスの濃度を測定する装置としては、窒素酸化物とアンモニアを含む測定ガスを取り込んで窒素酸化物検出器によって窒素酸化物濃度を測定する第1の測定系統と、測定ガスを取り込み、還元触媒を通して測定ガス中の窒素酸化物とアン

モニアを反応させた後の窒素酸化物濃度を窒素酸化物検出器で測定する第2の測定系統とを備えたものがある。還元触媒によってアンモニアと窒素酸化物を反応させるとアンモニア濃度に対応する窒素酸化物濃度が減少するので、第1の測定系統の窒素酸化物濃度から第2の測定系統の窒素酸化物濃度を引くとアンモニア濃度が算出される。

このようなアンモニアガス測定装置では、第1、第2の測定系統でリアルタイムに測定することができる利点をもつ反面、2台の窒素酸化物検出器を必要とするためコストが高くなる。また、2台の窒素酸化物検出器に直線性などに關し器差があれば、それがそのままアンモニア濃度測定の誤差となる。

他のアンモニアガス測定装置としては、測定ガスを導く第1のガス系統と、還元触媒を有し、測定ガス中の窒素酸化物とアンモニアを反応させる第2のガス系統とを備え、第1のガス系統と第2のガス系統を切り替えて窒素酸化物検出器に接続するものがある。その場合、両ガス系統の切り替え

は固定周期で行なわれる（例えば特開昭60-192257号公報参照）。

（発明が解決しようとする課題）

1台の窒素酸化物検出器をもつ測定装置では、低コストになり、検出器の器差を問題にする必要はないが、第1のガス系統と第2のガス系統は一方の測定中は他方の測定を行なうことができないため、測定中でない方のガス系統の検出出力がホールド状態となり、リアルタイムの計測を行なうことができない。

切り替えて測定を行なう装置では、第1のガス系統の窒素酸化物濃度と、異なる時間に測定された第2のガス系統の窒素酸化物濃度の差からアンモニア濃度を算出するので、切り替えの周期に対してアンモニア濃度の変動が大きい場合には誤差が大きくなる。また、算出されたアンモニア濃度は脱硝装置に添加するアンモニア量を調節するためのものであるため、残留アンモニア濃度の高い場合には短かい周期で切り替えて測定を行なう必要がある。

しかしながら、従来の装置では第1のガス系統と第2のガス系統の切り替えの周期は固定されている。

本発明はアンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの少なくとも1個の大きさに基づいて切り替え周期を変えることによって誤差の少ないアンモニアガス測定装置を提供することを目的とするものである。

（課題を解決するための手段）

第1図は本発明を概略的に表わしたものである。

1は測定ガスを導く第1のガス系統、3は還元触媒2を有し、測定ガス中の窒素酸化物とアンモニアを反応させる第2のガス系統、4は窒素酸化物検出器（NOx計）であり、5は第1のガス系統1と第2のガス系統3を切り替えて窒素酸化物検出器4に接続する切り替え手段である。6は切り替え手段5の動作を制御する制御部であり、制御部6は窒素酸化物検出器4の出力を取り込んでアンモニア濃度を算出する演算部7と、アンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度の

うちの少なくとも1個の大きさが大きくなると切り替え手段5の切り替え周期を短くするように切り替え手段5の切り替え周期を決定する切り替え制御部8とを備えている。

9はキーボードであり、このアンモニアガス測定装置の操作を行ったり、切り替え手段5の切り替え周期の標準値や、切り替え周期を変える場合のしきい値となるアンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの少なくとも1個の大きさなどを設定するものである。10は測定された窒素酸化物濃度や算出されたアンモニア濃度を表示する表示部である。

（作用）

アンモニア濃度の変動値によって切り替え周期を変える場合は、演算部7はアンモニア濃度の瞬時値と移動平均値を算出し、切り替え制御部8は瞬時値と平均値の差が設定されたしきい値を越えたときに切り替え周期を短くする。

アンモニア濃度によって切り替え周期を制御するときは、切り替え制御部8は演算部7からのアンモ

特開平2-120663 (3)

ニア濃度がしきい値を越えたときに切替え周期を短くする。

また、窒素酸化物濃度がしきい値を越えたときに切替え周期を短くすることもできる。

アンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの2個以上をしきい値と比較し、いずれか1個がしきい値を越えたときに切替え周期を短くするようにしてもよい。

(実施例)

第2図は一実施例を表わす。

11はプローブであり、煙道12中のガスを採取する。プローブ11には煙道12内のガスを直接取り込む第1のガス系統1と、還元触媒2を有し、取り込んだ測定ガス中の窒素酸化物とアンモニアを反応させる第2のガス系統3が設けられている。13はこのアンモニアガス測定装置のパネルの外側に設けられた前処理装置であり、各ガス系統1、3ごとにフィルタやバブリングセパレータを備え、取り込んだガス中の粗いゴミなどを除去する。

電磁弁5の切替え周期はアンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの少なくとも1個の大きさによって変化させられる。ただし、電源投入の直後は固定周期であり、また電磁弁15を切り替えて校正ガスを検出器4に導く校正中には電磁弁5の切替え周期の制御は行なわない。

一例として、キーボード9によってマイクロコンピュータ6に電磁弁5の切替えの標準周期を30秒とするように設定する。この標準周期は10秒～10分の範囲で任意に設定することができる。

また、アンモニアガス濃度の瞬時値と移動平均値の差がフルスケール(FS)の±5%を越えたときと、アンモニア濃度が5ppm以上になったときの少なくとも一方の条件が満たされたときは電磁弁5の切替え周期を30秒から15秒に短縮するように、キーボード9によってアンモニア濃度変動値のしきい値が±5%FS、アンモニア濃度瞬時値のしきい値が5ppmと設定する。これらのしきい値も任意に設定することができる。

14はこのアンモニアガス測定装置のパネルの内側に設けられた前処理装置であり、各ガス系統1、3ごとに電子クーラやドレンセパレータなどを備えて測定ガス中の水分や細かいゴミなどを除去する。

前処理装置14を経た第1のガス系統1と第2のガス系統3は切替え手段である電磁弁5に導かれる。電磁弁5の出口は校正ガスとの切替え用電磁弁15を経て窒素酸化物検出器のNOx計4に接続されている。電磁弁5は第1のガス系統1又は第2のガス系統3のいずれかを検出器4側に接続するものである。電磁弁15は測定ガス又は校正ガスを切り替えて検出器4に接続する。

検出器のNOx計4は例えば化学発光式の分析計であり、アンモニアガス測定装置で従来から用いられているものを使用することができる。

6は制御部としてのマイクロコンピュータであり、検出器4の出力信号を取り込んで窒素酸化物濃度とアンモニア濃度を算出するとともに、電磁弁5の切替えを制御する。

次に、第3図を参照して一実施例の動作について説明する。

電源投入から一定時間経過後、電磁弁5が開になっているのが第1のガス系統(NOx系)1と第2のガス系統(NH₃系)3のいずれであるかを判断し(ステップS1)、検出器4の出力信号を取り込む。

NOx系1が測定されているものとする、そのときのNOx値の瞬時値を表示する(ステップS2、S3)。設定された切替え周期が経過すると、そのときのNOxの瞬時値をホールドし(ステップS4、S5)、電磁弁5をNH₃系3に切り替える(ステップS6)。

検出器4の出力信号を取り込む(ステップS7)、このときの出力信号はNOxとNH₃が反応し、NH₃の分だけNOxが減少したものに对应する出力、すなわち(NOx-NH₃)が得られる。アンモニア濃度の瞬時値を出すために

$$NH_3 = NOx - (NOx - NH_3)$$

を演算し(ステップS8)、その値を表示する

特開平2-120663 (4)

(ステップS9)。

設定された周期が経過すると、アンモニア値の移動平均を算出する(ステップS11)。算出された移動平均とそのときのアンモニア瞬時値とを比較し(ステップS12)、その差が±5%FS以上でもなく、かつ、アンモニア瞬時値が5ppm以上でもない場合は次の周期は標準周期30秒のままとし(ステップS13、S14、S15)、アンモニア濃度の移動平均と瞬時値の差が±5%FS以上(ステップS13)、又はその差が±5%FS未満であってもアンモニア濃度瞬時値が5ppm以上である場合(ステップS14)は、次の周期を30秒から15秒に短縮する(ステップS16)。そのときのアンモニア濃度瞬時値をホールドし(ステップS5)、電磁弁5をNOx系位置に切り替える(ステップS6)。

その後は上記の動作を繰り返していく。

実施例ではアンモニア濃度変動値とアンモニア濃度瞬時値を用いて電磁弁5の切替え周期を制御しているが、NOx瞬時値の大きさが予め設定し

たしきい値を超えたときにも電磁弁切替え周期を短かくする機能を追加してもよい。

従来例として引用した特開昭60-192257号公報に記載のアンモニア濃度測定装置では、取り込んだ試料ガスにさらに窒素酸化物を添加している。本発明は引用例のように、さらに窒素酸化物を添加したガスを測定ガスとする場合にも適用することができる。

(発明の効果)

本発明ではアンモニア濃度変動値、アンモニア濃度及び窒素酸化物濃度のうちの少なくとも1個の大きさを用いて第1と第2のガス系統を切り替えるようにしたので、窒素酸化物検出器が1台であって低コストで器選を考慮する必要がない利点をもちながら、かつ、リアルタイムに近い正確なアンモニア濃度を測定することができる。

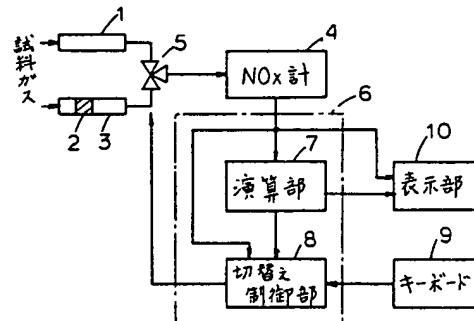
4. 図面の簡単な説明

第1図は本発明を示すブロック図、第2図は一実施例を示すブロック図、第3図は一実施例の動作を示すフローチャート図である。

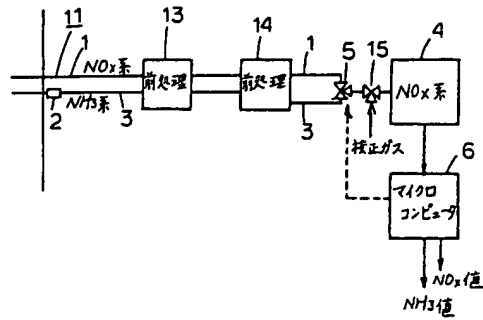
1……第1のガス系統(NOx)、2……還元脱硝酸触媒、3……第2のガス系統(NH₃)、4……窒素酸化物検出器、5……電磁弁、6……マイクロコンピュータ、7……演算部、8……切替え制御部、9……表示部、10……キーボード。

特許出願人 株式会社島津製作所
代理人 弁理士 野口繁雄

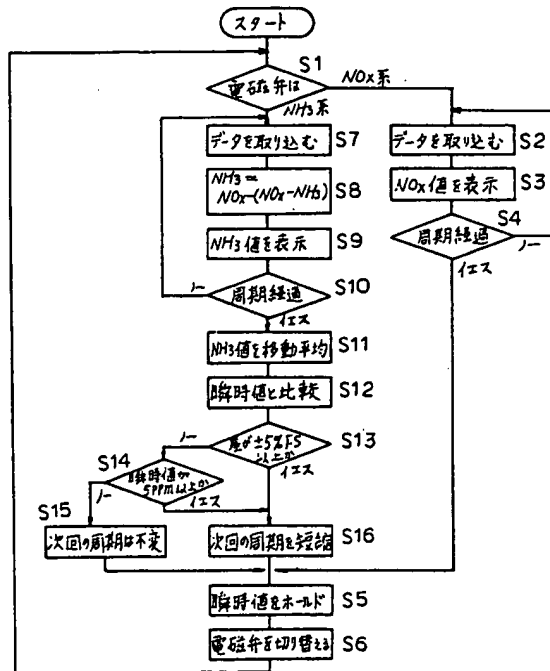
第1図



第2図



第3図



(19) 日本国特許庁 (J P)

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審査請求 未請求 請求項の数6 OL (全 5 頁)

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(33) 優先権主張国	ドイツ (DE)		

(54) 【発明の名称】 アンモニウムイオン定量装置と定量方法

(57) 【要約】

【課題】 上記ベルテロー法において使用が簡単で感度が高くかつ反射率計を用いる評価に適した手段と方法を提供する。

【解決手段】 フェノール誘導体で含浸した吸収性保持体。この保持体を次亜塩素酸塩またはその形成体を含有するアルカリ性試料溶液と接触させ、一定時間後に保持体の色の変化を評価する。

【特許請求の範囲】

【請求項1】 フェノール誘導体を含浸した吸収性保持体を含有することを特徴とするベルテロー法による水溶液中のアンモニウムイオンを定量する装置。

【請求項2】 吸収性支持体はさらに触媒と、さらに所望により錯化剤および緩衝物質を含有することを特徴とする請求項1に記載の装置。

【請求項3】 存在するフェノール誘導体は、そのアルキル基が1ないし6個の炭素原子を含有するヒドロキシフェニルアルキルアルコール、ヒドロキシフェニルアルキルカルボン酸またはヒドロキシ桂皮酸であることを特徴とする請求項1または2に記載の装置。

【請求項4】 存在するフェノール誘導体は、ヒドロキシ基が2または3の位置にあるヒドロキシベンジルアルコール、ヒドロキシフェニル酢酸またはヒドロキシ桂皮酸であることを特徴とする請求項1ないし3いずれか1項に記載の装置。

【請求項5】 2-ヒドロキシベンジルアルコールとニトロプルシドナトリウムを含有することを特徴とする請求項1ないし4いずれか1項に記載の装置。

【請求項6】 フェノール誘導体を含浸した吸収性保持体を次亜塩素酸塩または次亜塩素酸塩形成体を含有するアルカリ性試料溶液と接触させ、一定時間後に保持体の色の变化を評価することを特徴とするベルテロー法による水溶液中のアンモニウムイオンを定量する方法。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明はベルテロー法による水溶液中のアンモニウムイオンを定量する装置と方法に関する。

【0002】

【従来の技術】アンモニウム含量の定量は環境分析、特に水分析の非常に重要な日常業務となってきた。この定量は現在三つの異なった方法によって行われている。即ち

- アルカリ性媒体中でアンモニアを蒸留により分離し次で酸滴定を行う。
 - イオン選択的電極を用いる電位差測定。
 - 着色化合物生成後比色または光度測定。
- 【0003】色生成に基づく定量は近年重要性を増している。アンモニウムイオンに対して現在用いられている発色反応は通常ネスラー（Nessler）とベルテロー（Berthelot）の方法である。検出感度が高く、選択性も高くまた干渉に対する感受性が比較的低いために、特にベルテロー反応はアンモニウムイオンの検出法として確立されて来ている。適用分野は多岐にわたり、例えば、水、食物、土壌抽出物、生体材料等の中のアンモニウムイオンの定量があげられる。

【0004】アンモニウムイオン、次亜塩素酸塩とフェノールを混合すると青色が生ずることはベルテローによって早くも1859年に記述された。反応機構の解明は

その後多くの研究（Anal. Chem. 49, 464（1977））の課題であった。反応進行の必要条件は使用するフェノールのパラ位置が自由なことである。使用する次亜塩素酸塩源および使用するフェノール成分によるが、最適反応はpHや試薬添加の時系列などの特性的反応条件を厳守する必要がある。使用するフェノール成分は通常フェノールそのものやサリチル酸およびチモールである。高い検出感度や高い反応速度に関して、既存技術では一連の他のフェノール誘導体が、そのアンモニウムイオンの定量的検出の適性について、詳細に検討されている。この中で2-メチルフェノール、2,6-ジメチルフェノール、2-クロロフェノール、2,6-ジクロロフェノール、グアヤコール、o-フェニルフェノール、m-クレゾール、1-ナフトールおよび2-メチル-5-ヒドロキシキノリンは特に使用可能であることが分っている（Analyst 109, 549（1984））。

【0005】連続測定方式や市販のテストキットでの使用を可能にするために、適当な試薬と反応条件を選ぶことによってベルテロー反応を最適化する多くの試みがなされてきた。しかしながら、ベルテロー反応の使用は今日迄湿式化学、すなわち液体反応物のみが用いられる反応、の領域に留まっていた。

【0006】しかし近年固体吸収性保持体、いわゆるテストストリップ（試験固片）を用いる分析が重要性を増している。テストストリップを使用する大きな利点として、特に、取扱いが簡便なことや試薬が少量であるため廃棄に問題を生じないことなどがあげられる。このストリップでは、検出反応に必要な試薬の全部または一部を吸収性または膨潤性保持体またはフィルムに適用する。反応帯が試料と接触すると、検出反応は進行する。色検出反応が進行する。生じた色は測定すべき被分析物の量の尺度であり、比色目盛によって目視的に、あるいは簡単な反射率計を用いて評価することができる。

【0007】ネスラー反応に基いてアンモニウムの量を検出するテストストリップは知られているが、これらは20ppm以上の比較的高いアンモニウムイオン含量の検出にのみ適している。水試料のアンモニウムイオン濃度は通常低いので従ってテストストリップはあまり用いられない。多層テストストリップ方式は血漿中のアンモニウムイオンの定量のために存在するが、この方式における検出はpH指示薬（プロモフェノールブルー）の色の变化に基いている。

【0008】

【発明が解決しようとする課題】本発明の目的は使用が簡単で感度が高く特異的でありまた反射率計を用いる評価に適した、ベルテロー法による水溶液中のアンモニウムイオン定量の装置および方法を提供することである。

【0009】

【課題を解決するための手段】本発明はフェノール誘導

体を含浸した吸収性保持体を含むことを特徴とする、ベルテロー法による水溶液中のアンモニウムイオンを定量する装置を提供する。

【0010】更に本発明はフェノール誘導体を含浸した吸収性保持体を次亜塩素酸塩または次亜塩素酸塩形成体を含むアルカリ性試料溶液と接触させ、一定時間後に保持体の色の変化を評価することを特徴とするベルテロー法による水溶液中のアンモニウムイオンを定量する方法を提供する。

【0011】

【発明の実施の形態】アンモニウムイオンの定量的検出用の先行技術に記載されたフェノール類は、貯蔵安定性、検出感度、反応速度、好ましくない副反応、生じたインドフェノールの色の安定度、毒性、測定の再現性などの種々の理由から、ベルテロー反応を固体のテスト保持体に移行させるには不適当であることが立証されている。特に、色の生成や反応速度の点では最も適当なフェノール類は、余りにも揮発性であり保持物質に対して必要な親和力をもっていない。このため、とくに、テスト

ストリップ貯蔵用の容器を開けるといふ強い臭気が発生する。

【0012】驚くことにヒドロキシ基が2または3の位置にありアルキル基が1ないし6個の炭素原子を有するヒドロキシフェニルアルキルアルコール、ヒドロキシフェニルアルキルカルボン酸、ヒドロキシ桂皮酸などのフェノール誘導体が発明の手段として適していることが分った。適当なフェノール誘導体として、例えば、ヒドロキシベンジルアルコール、ヒドロキシフェニル酢酸、ヒドロキシ桂皮酸、2-(2-ヒドロキシフェニル)エタノール、2-(3-ヒドロキシフェニル)エタノール、3-(2-ヒドロキシフェニル)プロパノール、4-(2-ヒドロキシフェニル)ブタノール、3-(2-ヒドロキシフェニル)プロピオン酸、4-(2-ヒドロキシフェニル)酪酸、5-(2-ヒドロキシフェニル)吉草酸などがあげられる。この中で2-ヒドロキシベンジルアルコール、2-ヒドロキシフェニル酢酸、ヒドロキシ桂皮酸が好ましく、特に2-ヒドロキシベンジルアルコールが好ましい。これらの化合物を含む本発明の吸収性保持体は室温で1年以上貯蔵できる。

【0013】使用可能な吸収性保持体とはこのようなテストに慣例的に用いられるすべての保持体である。濾紙が最も広く用いられるが、他の吸収性のセルローズまたはプラスチック製品を使用することも可能である。吸収性保持体、好ましくは濾紙はアンモニウムイオンの定量に必要な試薬の1部を含む含浸溶液でそれ自体知られた方法によって含浸される。含浸乾燥した濾紙は正方形または矩形の区分に分けることができ、この区分を続いて既知の方法でプラスチックフィルム、紙ストリップまたは金属ストリップ上に接着剤で密着または固着させることができる。

【0014】また吸収性保持体を含浸前にテープ状でプラスチックバンドに貼り付け、含浸後にテープ方向に垂直に切断して扱いやすいストリップとすることもできる。

【0015】吸収性保持体がフェノール誘導体のみならず触媒も含有することは有利なことである。必要ならば、保持体はまた錯化剤や緩衝物質を含有することができる。適当な触媒にはニトロアルシドナトリウム、マンガン(II)塩または亜鉛塩があり、ニトロアルシドナトリウムが好ましい。含浸溶液は約0.05ないし0.2

10 %, 好ましくは0.1%のニトロアルシドナトリウムを含有する。

【0016】上述の錯化剤と緩衝物質は吸収性保持体上に存在してもよいあるいは試料溶液に加えてもよい。試料溶液に加える方がより有利であることが分っている。

【0017】試料の妨害置換基を錯化するために、試料溶液を例えば1-ヒドロキシエタン-1, 1-ジホスホン酸、シクロヘキシルジアミノテトラ酢酸、シトレートまたはEDTA、好ましくは1-ヒドロキシエタン-1, 1-ジホスホン酸と混合する。試料溶液は約2ないし10%, 好ましくは5%の1-ヒドロキシエタン-1, 1-ジホスホン酸を含有する。

【0018】試料溶液にpH範囲を10-12に維持できた検出反応を妨害しない緩衝物質を加える。適当な緩衝系は吸収性保持体にも適用できる緩衝系である。用いる緩衝濃度は試料溶液のpHとその中に存在する遊離の酸または塩基による。適当な緩衝液として、例えば、水酸化ナトリウム/酒石酸ナトリウム緩衝液、水酸化ナトリウム/硼酸ナトリウム緩衝液、炭酸ナトリウム/炭酸水素ナトリウム緩衝液があり、水酸化ナトリウム/酒石酸ナトリウム緩衝液が好ましい。

【0019】この特定の緩衝系を用いてpHを約11とした試料溶液を次亜塩素酸塩または次亜塩素酸塩形成体と混合する。この目的に適した公知の次亜塩素酸塩形成体は、例えば、ジクロロイソシアヌル酸、トリクロロイソシアヌル酸、クロラミンT、および塩素水溶液である。次亜塩素酸塩のかわりに次亜臭素酸塩もまた用いることができる。本発明によれば、ジクロロイソシアヌル酸と次亜塩素酸ナトリウムが好ましい。

40 【0020】アンモニウムイオンの定量を行うために、吸収性保持体を、反応帯が完全にぬれるように、2ないし20分間、好ましくは約8分間アルカリ性の次亜塩素酸塩含有試料溶液中に置く。次にこのテストストリップを試料溶液からとり出し、強く水切りをして、生じた発色を反射率計を用いてまたは比色目盛によって評価する。本発明の方法では、公知の方法と比べて、テストストリップを用いて水溶液中のアンモニウムイオンを簡単、正確かつ迅速に定量することができ、0.2ないし10mg/lの濃度の定量が可能となる。

50 【0021】

【実施例】

実施例1

沓紙 (Scholler & Hosch 300A) を下記の試薬溶液で含浸し、次いで含浸後温風を用いて乾燥した: 100 g の水中に 3.5 g の 2-ヒドロキシベンジルアルコールと 0.1 g のニトロアルシドナトリウム。

【0022】得られた沓紙を既知の方法で保持材、例えばポリエステルフィルムに貼り付けた。

【0023】アンモニウムイオン含量が 0 ないし 10 mg/l, pH が 11 で、溶液 5 ml 当たり 1 mg のジクロ*

a) 目視比色評価:

濃度	0	0.5	2.5	5.0	10.0
(mg/l)					
色	無色	淡緑色	青緑色	淡青色	青色

この実験からアンモニウムイオンの濃度が変わるとかなり異なった発色を生じ従ってアンモニウムイオン濃度は適当※

b) 反射率評価:

濃度	0	0.25	0.5	1.0	2.5	3.0	5.0	7.5	10.0
(mg/l)									
相対反射率	74.8	72.7	69.5	63.5	53.6	42.4	28.2	18.4	13.7
(%)									

上に測定した反射率-濃度曲線 (検量線) をバーコード読み取り方式を用いて反射率計に読み込み、使用濃度と測★

*ロイソシアヌル酸を含有する標準アンモニウムイオン溶液を調製した。テストストリップを溶液に入れ、8分後に取り出し、水切りをして、簡単な反射率計を用いて相対反射率を測定してまた目視比色法によって評価した。

【0024】pHを規定する緩衝溶液は 100 g の水中

44 g の酒石酸ナトリウムカリウム

9 g の NaOH ペレットおよび 5 g の 1-ヒドロキシエタン-1, 1-ジホスホン酸ナトリウム塩を含有する。

※な色目盛を用いる目視比色法によって定量できることが分る。

★定濃度の関係を測定した。

【0025】

使用濃度 (mg/l)	0.5	1.0	2.5	6.5
測定濃度 (mg/l)	0.5	1.0	2.5	6.2
	0.5	1.0	2.4	6.5
	0.5	0.9	2.5	6.6
	0.5	1.1	2.4	6.8
	0.5	1.0	2.6	6.3

この結果が示すように、反射率-濃度曲線は感度がよく合せて検出反応の再現性も高いため、アンモニウムイオンの非常に高感度かつ正確な定量が可能になった。

【0026】フェノール誘導体として 2-ヒドロキシベンジルアルコールのかわりに 2-ヒドロキシフェニル醋酸またはヒドロキシ桂皮酸を用いても類似の結果が得られた。

実施例2

9つの異った廃水試料をアンモニウムイオンについて反射率計を用いて実施例1と同様な方法によって分析した。比較のために試料を従来の光度測定法で分析し次の結果を得た。

【0027】

☆

試料	反射率測定 (mg/l)	光度測定 (mg/l)
1	3.8	3.5
2	4.6	4.8
3	4.9	5.1
4	2.6	2.4
5	4.6	4.5
6	4.2	4.1
7	0.5	0.4
8	0.6	0.6
9	0.6	0.7

既存の方法と対照的に、テストストリップを用いる方法では試料水溶液中で簡単、正確かつ迅速なアンモニウムの定量が可能になる。

実施例3

沓紙 (Scholler & Hosch 300A) を下記2溶液に引続いて含浸し、各含浸後温風を用いて乾燥した。

溶液1: 100 g の水中

50 3.5 g の 2-ヒドロキシベンジルアルコールと 0.1

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特開平8-193989

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gのニトロプルシドナトリウム。

溶液2: 100gの水中

10gの酒石酸ナトリウムカリウム

2gのNaOHペレットと1.1gの1-ヒドロキシエ
タン-1, 1-ジホスホン酸ナトリウム塩。

【0028】検出を実施例1記載のように行った。実施

8

例1の結果と類似の結果が得られた。

【0029】

【発明の効果】本発明の方法では、既存の方法と比べ
て、テストストリップを用いて水溶液中のアムモニウム
イオンをより簡単、正確かつ迅速に定量することができ
る。

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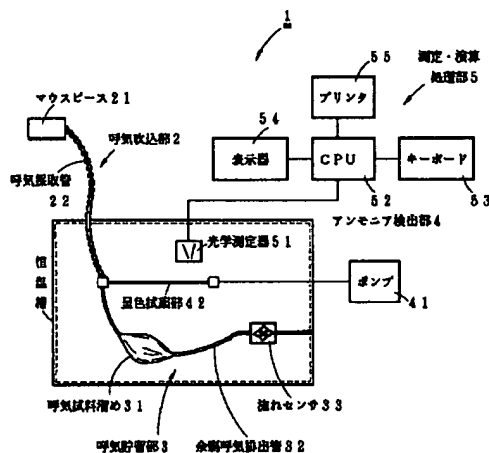
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(54)【発明の名称】 呼気中アンモニア測定方法及び装置

(57)【要約】 (修正有)

【目的】呼吸を、終末呼吸のみ、しかもその中に含まれるアンモニアの吸着や消耗がないように正確にサンプリングし、呼吸中アンモニア濃度を簡便にしかも高密度高精度に測定する技術を提供する。

【構成】被検者が呼出する呼吸を体温或いはそれ以上の温度に加温した状態で可変容積型の呼吸試料溜めに送り込み、初期の呼吸は呼吸試料溜めから排出するとともに終末呼吸を呼吸試料溜めから一定量吸引してアンモニア呈色試薬部に供給し、試薬部の呈色の度合いを光学的に測定して呼吸中のアンモニア濃度を求める。



【特許請求の範囲】

【請求項1】 被検者が呼出する呼吸を体温或いはそれ以上の温度に加温した状態で可変容積型の呼吸試料溜めに送り込み、初期の呼吸は呼吸試料溜めから排出するとともに終末呼吸を呼吸試料溜めから一定量吸引してアンモニア呈色試薬部に供給し、試薬部の呈色の度合いを光学的に測定して呼吸中のアンモニア濃度を求めることを特徴とする呼吸中アンモニア測定方法。

【請求項2】 呼吸試料溜めからの呼吸の排出を流れセンサーでチェックし、該センサーの出力が停止した後一定時間試料吸引ポンプを作動させるものである請求項1記載の呼吸中アンモニア測定方法。

【請求項3】 試薬部として、市販のガス検知管を使用するものである請求項1記載の呼吸中アンモニア測定方法。

【請求項4】 試薬部として、カセットタイプで呈色試薬として遷移金属イオンを含浸させた濾紙を使用するものである請求項1記載の呼吸中アンモニア測定方法。

【請求項5】 内壁加温機能を備えた呼吸採取管とマウスピース或いは呼吸採取マスクから構成される呼吸吹込部と、該吹込部から供給される呼吸を加温状態で一時的に貯留する可変容積型の呼吸試料溜めと該呼吸試料溜めから余剰の呼吸を排出する余剰呼吸排出管から構成される呼吸貯留部と、貯留した或いは呼吸採取管の基部に残存する呼吸の一部を一定量吸引するポンプと吸引途中において試料中のアンモニアと反応して呈色する試薬部から構成されるアンモニア検出部と、試薬部の呈色の程度を光学的に測定し、該測定信号を演算処理して予め記憶させている検量線から呼吸中のアンモニアガス濃度を算出し、臨床検査データとして記憶し或いは出力装置に信号を出力する測定・演算処理部を含んで構成されることを特徴とする呼吸中アンモニア測定装置。

【請求項6】 呼吸試料溜めは薄膜製のバッグであり、該呼吸試料溜めの先端部に呼吸採取管、後端部には余剰呼吸排出管をそれぞれ連結し、該余剰呼吸排出管には呼吸流出をチェックする流れセンサーを組み込んでなる請求項5記載の呼吸中アンモニア測定装置。

【発明の詳細な説明】

【0001】

【産業上の利用分野】本発明は、呼吸中アンモニアを測定する方法及び装置の改良に係わり、特に呈色試薬を用いるものに関する。

【0002】

【従来の技術】血中アンモニア濃度は、肝硬変やアルコール性肝症など多くの肝疾患、蛋白質代謝や運動代謝の異常等で増加することが知られている。アンモニアは、強い毒性を示すため濃度が高い場合には昏睡や意識混濁等の中毒症状を呈することもある。そのため、従来から血中アンモニア濃度を測定する種々な手法が開発されているが、これらはいずれも特殊な分析用具や高度な技術

を必要とした手間もかかる難点を有している。しかも、血中アンモニア量は一般に微量でしかも採血後放置することにより濃度が増加するし妨害物質も存在するので、精度良く測定することは困難であり、特定の施設でしか測定されていないのが現状である。

【0003】一方、呼吸中アンモニア濃度は血中の遊離アンモニアレベルを反映することが知られている。即ち、アンモニアの肺胞膜における拡散能は酸素の3万倍、炭酸ガスの1,500倍であり両者に比べてはるかに肺胞膜を透過しやすいと考えられており、肺胞アンモニア分圧と静脈血アンモニア分圧とはほぼ等しいと見做すことが出来る。また、呼吸は血液と異なり無侵襲で採取できる利点がある。

【0004】そこで、従来から呼吸中アンモニアを測定することが古くから試みられているが、現在までの報告例は極めて少ない(Jacucz J.A., SCIENCE, 129, 269, 1959, Robin E.D., ibid. 129, 270, 1959)。これにはいろいろの理由が考えられるが、やはりアンモニアが水に溶けやすくて物質との反応性が高いため、吸着等で損失するためと思われる。更に、呼吸の採取法や測定法上の問題もあり、測定値がバラついて信頼性が乏しいこともある。

【0005】このような事情から、現在でも呼吸中アンモニアは全く日常的には測定されておらず、只研究目的で汎用ガスクロマトグラフィーを用いて呼吸を大量に冷却トラップする形で測定されているに過ぎない。この種報文ではケミルミネッセンス法を用いた呼吸中アンモニアの測定装置の報告がある(Larson, T.V., et al, Respi rat. Environ. Exercise Physiol., 46 (3), 603-607, 1979)。この方法は、呼吸を加熱チューブで装置に導入し、高温反応管でアンモニアを酸化してNOに変換してこれにオゾンと反応させ、発生する発光の強度を光電子倍增管で検出してアンモニア濃度を求めるものである。この方法は極めて高感度であるが、大型の装置と専門のオペレーターを必要とするため、実用化と普及が妨げられている。また、研究レベルで分光学的に測定する方法も報告されているが、単に報告のみで終わっている(Hunt R.D., et al, Amc. Labo., June, 10-23, 1977)。

【0006】

【発明が解決しようとする課題】上述した通り、肝性疾患特に肝性昏睡(Coma)と血中アンモニアとの関係は昔から注目されているが、種々な研究開発にもかかわらずアンモニアの物理化学的特性により、未だ実用化に至っていないし、まして臨床検査手技として現場では全く用いられていない。そこで本発明者は、呼吸中アンモニアの臨床検査的観点から呼吸中アンモニアの測定に関して問題分析を行なった。その結果、現在かかえている問題は次の2点に集約されることが明確となった。

(1)呼吸採取法の簡便化とアンモニア成分の回収の信頼性

(2) アンモニア検出の高感度化と測定精度の確保

【0007】

【課題を解決するための手段】本発明者は上記問題点について鋭意研究の結果、本発明を完成させたものである。まずアンモニアロスを考慮に入れた呼気の採取に関しては、

- (a) 吸着性のないバッグに吹き込む
- (b) 酸性溶液が冷凍された容器へ吹き込む
- (c) 加温チューブを使用し、口から直接検出系（装置）へ吹き込む

等の方法が考えられる。本発明では、この(c)を採用し更に工夫を加えた。即ち、(a)及び(b)の場合には、装置の他に別の容器が必要になるだけでなく、検出系へ被検試料を持ち込まなければならず、新たな別の操作が加わる。一方(c)の場合は、呼気（呼出）ガスを直接分析装置に吹き込むので、被検者自らがアンモニア測定をすることが可能になり、臨床検査としてアンモニア測定を実施することを前提に考えれば、実用化にとって大変重要な要素手技である。

【0008】更に、呼気を採取する場合常に留意しなければならないことは、気道空間（Dead space）にある呼気の取扱いである。この部分の呼気は、肺胞気からの“呼気”と吸入された“大気”が混ざったもので、正しい呼気（肺胞気）として扱うことはできない。この気道空間の呼気は約150mlとされ、最初の吹込部分（初期呼気）は試料として取り扱ってはならず、捨てる必要がある。つまり呼気試料は、これを除いた終末呼気でなければ、信頼性が得られない。

【0009】アンモニアを正確に測定するためには、アンモニアが種々の物質に溶解しやすく、ロスし易いという特性をよく知り、これを克服する工夫が必要である。また呼気中には数%の炭酸ガスが含まれているので、そこに水分が介在するとアンモニアはたやすく損失してしまう。Hamiltonは、これを回避するために苛性ソーダなどの強アルカリ吸湿剤を用いて炭酸ガスと水を同時に除去する方法を提示している（Hamilton L.H., US Patent No.4,947,861 1990）。

【0010】しかしこの方法は、別の消耗品（吸着剤）を必要とするしまたその取扱いのため測定操作が煩雑になる。そこで本発明では、上記アンモニアの回収の点も考慮して、呼気が接触する呼気採取管及び呼気試料溜めの部分、好ましくは装置の要部を恒温槽内に収納し、体温或いはそれ以上の温度例えば40～50℃に加温して、アンモニアと水や炭酸ガスとの反応による損失を防止することにした。

【0011】本発明の呼気中アンモニア測定方法及び装置は、検体として人（或いは動物）の呼気を採用し、1回の呼出で呼気中のアンモニア濃度を測定する無侵襲な臨床分析方法及び装置である。以下図面に示す実施例に基づいて本発明を詳細に説明する

【0012】

【実施例】図1は、本発明に係る呼気中アンモニア測定装置1のブロック図を示す。この測定装置1は、呼気吹込部2、呼気貯留部3、アンモニア検出部4及び測定・演算処理部5から構成されている。

【0013】呼気吹込部2は、呼気捕集器としてのマウスピース21を呼気採取管22の先端に取り付けたものから構成される。呼気採取管22は、例えば内径が1～5mm程度長さが1m前後のテフロン管の外周にヒータと保温材を被せたものからなり、その内部を加温して呼気中の水分の付着を防止する。加温は、コントローラで36～100℃の任意の温度例えば40℃に調節して行なう。マウスピース21の代わりに呼気採取マスクを用いてもよい。

【0014】呼気貯留部3は、呼気試料溜め31と余剰呼気排出管32からなる。呼気試料溜め31は弾力性のある材料或いは収縮機能をもっているゴムなどの薄膜製バッグからなる可変容積型のものであり、その先端部は呼気採取管22に、後端部は余剰呼気排出管32にそれぞれ連結されている。また該余剰呼気排出管32には、呼気流出をチェックする流れセンサー33が組み込まれている。呼気試料溜め31の最大容量は、アンモニア検出部4の容量にもよるが、200～800ml程度が適当である。この呼気試料溜め31の形状は、薄手のプラスチックシートで直径が3～4cmの円筒型（ソーセージ型）とするのが最も好ましい。尚、適当な重さの板を乗せるとか適当なスプリングで挟み膨らんだ形状のものがゆっくりと試料ガスを押し出すようにしてもよい。

【0015】尚、人の1呼吸は約1リットル程度であるので、呼出された呼気は呼気試料溜め31を最大容量に膨らませ、なおかつ余剰の呼気は余剰呼気排出管32から排出される。従って、ワンブレスの後には、呼気試料溜め31内には終末呼気のみが貯まることになる。一方、余剰呼気排出管32に組み込まれた流れセンサー33は、余剰呼気排出管32からの呼気の排出が続いている間出力をだし、排出が止まる（即ちワンブレスの完了）と出力も止まる。

【0016】アンモニア検出部4は、呼気試料溜め31に貯留した或いは呼気採取管22の基部に存在する呼気の一部（終末呼気）を一定量吸引するポンプ41と、吸引途中において試料中のアンモニアと反応して呈色する試薬部42から構成される。そしてポンプ41は、前記流れセンサー33の出力がとまった時点から一定時間作動するようになっている。このとき、呼気試料溜め31はその内部の呼気を押し出す作用をする。つまり、呼気試料溜め31は常に正圧になっており、ポンプ41の吸引により大気が混入しないことが本発明の重要な工夫の一つとなっている。

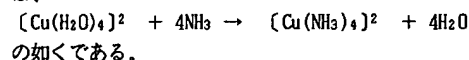
【0017】呼気中アンモニア濃度範囲は、健康者では通常0.1～0.3ppm程度とされているが、病的になれば

5ppm 以上になることも珍しくない。従って、本発明における試薬部42として、市販のガス検知管（メーカー：光明理化学、ガステック）が使用可能である。

【0018】測定・演算処理部5は、試薬部42の呈色の程度を光学的に測定する光学測定器51、該測定器51からの測定信号を演算処理して予め記憶させている検量線から呼気中のアンモニアガス濃度を算出し、臨床検査データとして記憶し或いは出力装置に信号を出力するなど装置全体の作動プログラムを管理するマイクロコンピュータ52、キーボード53、表示器54、プリンター55等から構成される。

【0019】市販のガス検知管は、本発明における通常測定域では分解能が幾分悪い。そこで、図2に示すような構造のものを開発した。この試薬部6は、ホルダーベース61に設けた陥凹部62に網製の支持層63とリング64、呈色試薬を含浸させた発色層65、リング66及び透明シート67を順次組み込んだもので、ホルダー61の側面に設けた試料入口68から底面に設けた試料出口69まで試料ガスを吸引する間に試料中のアンモニアガスと発色層65とを反応させるものである。この発色層65に使用する試薬としては、アンモニアはアルカリ性を示すのでその吸収でpHが変化することから、pH指示薬を使用するのが好ましい。例えば、フェノールフタレイン（8.0～9.6）、ニュートラルレッド（6.8～8.0）、プロモチモールブルー（6.1～7.6）、プロモクレゾールパープル（pH8.2で反応）等である。

【0020】更に本発明では新たに発色剤を研究し、アンモニアと呈色ししかも発色試薬が安定な特性のものを開発した。それらは、アンモニアと錯体形成によることを特徴とするものである。この試薬は、呼気中に現出したアンモニアと特異的、且つ迅速に反応が終了するのが特徴である。呈色試薬としては、例えば、 Cu^{2+} 、 CO^{3+} 、 Ni^{2+} などの遷移金属イオンを含んでいるものである。それは単に CuSO_4 や $\text{Ni}(\text{NO}_3)_2$ の水溶液をセルロース濾紙に含浸させたものでもよいが、増感するために特定のリガンドを結合させたものでもよい。例えば、



【0021】本発明では、呈色した試薬部を目視して数値化（濃度の読み取り）をすることも考えられるが、臨床検査手技としての実用化を考えたとき、この呈色部を光学的に数値化して濃度表示する法が望ましい。光学的方法としては、反射光（率）の測定が实际的である。

【0022】

【発明の効果】以上説明したように本発明によれば、呼気中アンモニア濃度を簡単な操作で迅速に求めることが

可能となる。呈色試薬は、取扱いやすいカセットタイプとなっており、また市販のガス検知管も使用することができる。呈色した部分は自動的に光学的反射計で濃度記録するものである。本発明により、さらに以下の如き便益がもたらされる。

1) 呼気を一吹きするだけで、呼気中のアンモニア濃度、即ち血液採取せずとも血中アンモニアレベルが判る。このことにより、採血具が不要であるだけでなく、患者の肉体的、精神的負担を軽減することができる。そして、血液による感染も危惧する必要がなくなる。

2) 測定操作は、所定の試薬部を装置にセットし、呼気を吹き込むだけであるから、特別な操作担当者が不要となり、新しい検査としてルーチン化されても医療従事者の負担にならない。また、測定の結果は2～3分程度で判明し、そのデータが自動記録されるので、診療にすぐ対応でき、効率的になる。

3) 測定装置は小型軽量であり、100V商用電源があれば場所を選ばず測定が可能となる。また付属品も特別なものは不要であり、使用場所の制限もないことから、アンモニアの測定に於ける将来必要とされる診療に役立つものである。

4) 装置は部品構成が簡単であるので、低価格で製作できる。消耗品としての試薬部も安価であるので、測定コストは極めて安価となる。

5) 無侵襲であるため、繰り返し測定が容易に行え、スクリーニングや治療中のモニターなどに効果的に活用され、成人病等の低減に役立つものである。

【図面の簡単な説明】

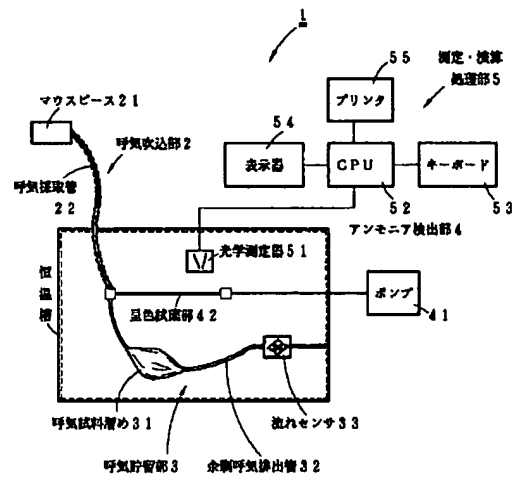
【図1】本発明に係る呼気中アンモニア測定装置の一例を示すブロック図である。

【図2】試薬部の他の例を示す分解斜視図である。

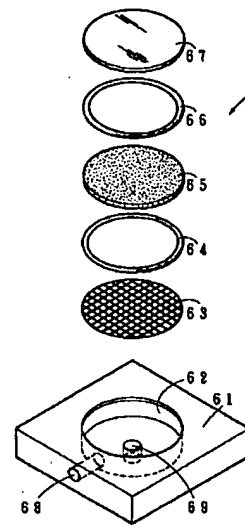
【符号の説明】

- 1 呼気中アンモニア測定装置
- 2 呼気吹込部
- 21 マウスピース
- 23 呼気採取管
- 3 呼気貯留部
- 31 呼気試料溜め
- 32 余剰呼気排出管
- 33 流れセンサー
- 4 アンモニア検出部
- 41 ボンプ
- 42 試薬部
- 5 測定・演算処理部
- 51 光学測定器
- 52 マイクロコンピュータ
- 6 試薬部

【図1】



【図2】



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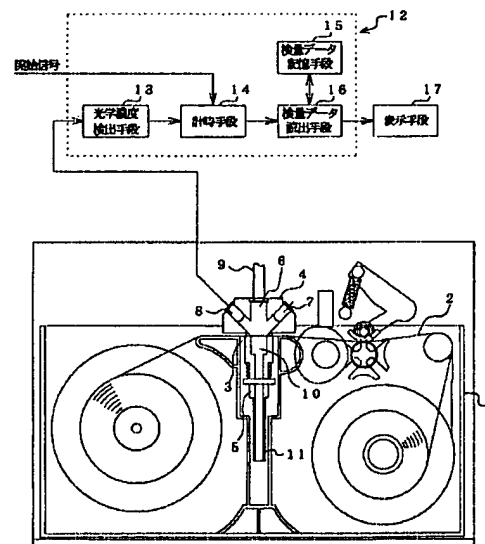
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(54)【発明の名称】 呈色反応テープ式アンモニアガス測定装置

(57)【要約】

【課題】 検出テープの検出感度に拘束されることなく、低い濃度のガスを測定すること。

【解決手段】 ガス検出テープ2の搬送路に対向して配置された発光ダイオード7とフォトダイオード8を収容し、被測定環境のガスをガス検出テープ2に供給するガス導入口6を有する測定ヘッド4と、測定開始により作動し、またフォトダイオード8からの信号が基準値に一致した時点で停止する計時手段14と、計時手段の時間を検量データに基づいてアンモニアガスの濃度に変換する検量データ読出手段16と手段とを備え、環境に晒されても変色しない程度の検出テープに対してフォトダイオード8の信号が基準値に到達するまでサンプリングを継続することにより、極めて濃度の低いアンモニアガスにより反応痕を生じさせる。



【特許請求の範囲】

【請求項1】 ガス検出テープの搬送路に対向して配置された発光手段と受光手段を収容し、被測定環境のガスをガス検出テープに供給するガス導入口を有する測定ヘッドと、測定開始により作動し、また前記受光手段からの信号が基準値に一致した時点で停止する計時手段と、前記計時手段の時間を検量データに基づいて被検ガスの濃度に変換する手段と、を備えてなる呈色反応テープ式アンモニアガス測定装置。

【発明の詳細な説明】

【0001】

【発明の属する技術の分野】本発明は、大気などの気体中に存在するアンモニアガスを検知紙上の呈色反応として検出する測定装置に関する。

【0002】

【従来の技術】例えば半導体製造工程等のクリーンルームにあっては、人体や壁材から放出される極僅かなアンモニアガスが製品の品質を大きく左右するため、特開平7-83911号公報に見られるようにフルオレセイン系染料と、環境中の被検ガス等による反応を防止するバッファ成分としての強酸性有機酸とを保湿剤とともに紙葉体に担体に担持させた検知紙を用い、被検ガスを検知紙を透過させることにより塩基性ガスが保湿剤に保持されている水分に溶解して紙葉体をアルカリ側に変移させ、フルオレセイン系染料を水素イオン濃度に対応させて発色させて検出するガス検出紙が提案されている。

【0003】

【発明が解決しようとする課題】このような検出紙は、強酸性有機酸の濃度を下げることにより検出感度を上げることができるものの、環境中に含まれる成分の影響を受けて未使用領域に変色を来して測定結果に誤差を招くという問題がある。本発明はこのような問題に鑑みてなされたものであって、その目的とするところは環境中の被検ガスによる変色を防止しつつ、極めて低い濃度のアンモニアガスを測定できる呈色反応テープ式アンモニアガス測定装置を提供することである。

【0004】

【課題を解決するための手段】このような問題を解消するために本発明においては、ガス検出テープの搬送路に対向して配置された発光手段と受光手段を収容し、被測定環境のガスをガス検出テープに供給するガス導入口を有する測定ヘッドと、測定開始により作動し、また前記受光手段からの信号が基準値に一致した時点で停止する計時手段と、前記計時手段の時間を検量データに基づいて被検ガスの濃度に変換する手段とを備えるようにした。

【0005】

【作用】環境に晒されても変色しない程度の感度を有す

るアンモニアガス検出テープを用いても、受光手段の信号が基準値に到達するまでサンプリングを継続して積分効果を十分に活かし、もって極めて濃度の低いアンモニアガスにより反応痕を生じさせる。

【0006】

【実施例】そこで以下に本発明の詳細を図示した実施例に基づいて説明する。図1は本発明の一実施例を示すものであって、カセット1は、フルオレセイン系染料と、環境中の被検ガス等による反応を防止するバッファ成分としての強酸性有機酸とを保湿剤とともに紙葉体に担体に担持させたアンモニアガス検出テープ2を収容して構成され、その窓3の両側にテープ2を挟むように測定ヘッド4と、吸引ヘッド5とが配置されている。

【0007】測定ヘッド4は、被検出ガスの導入口6が形成された遮光容器として構成されていて、内部に発光ダイオード7とフォトダイオード8とが、検出テープ2上に形成された反応痕を検出できるように入射関係を持たせて収容され、パイプ9により被測定環境に連通するように構成されている。

【0008】吸引ヘッド5は、導入口6と対向するように流出口10を穿設がされ、パイプ11を介して図示しない吸引ポンプからの負圧を受けている。

【0009】図中符号12は、信号処理装置で、フォトダイオード8からの信号が基準値に一致した場合に信号を出力する光学濃度検出手段13と、測定開始信号により作動し、また光学濃度検出手段13からの信号により計時動作を停止する計時手段14と、図3に示したようにサンプリング時間とガス濃度との関係、つまり検量線データを格納した検量データ記憶手段15と、計時手段14の計時時間に基づいて記憶手段15からガス濃度を読み出して表示手段17に出力する検量データ読出手段16とから構成されている。

【0010】この実施例において、カセット1の窓3から露出している領域の検出テープ2を測定ヘッド4と吸引ヘッド5とで挟持し、測定を開始すると（ステップイ）、計時手段14が帰零されてから計時動作を開始し（ステップロ）、また図示しない吸引ポンプを作動させる。

【0011】被検ガスは、パイプ9を経由して測定ヘッド4に被測定ガスが吸い込まれ、測定ヘッド4から検出テープ2を通過して吸引ヘッド5に移動する過程で検出テープ2に含浸されている薬剤と反応してこれの表面にアンモニアガスの濃度と時間との積に対応した濃度で反応痕を生じさせる。

【0012】この過程で発光ダイオード7から放射された光は、検出テープ2の表面に形成された反応痕の光学的濃度に応じて吸収を受けて反射され、フォトダイオード8に入射して電気信号に変換される。光学濃度検出手段13は、フォトダイオード8からの信号と基準値とを比較し、一致した時点で（ステップハ）信号を出力し

3

て計時手段14の計時動作を停止させる(ステップニ)。

【0013】検量データ読出手段16は、計時手段14に計時されている時間に一致する濃度を検量データ記憶手段15から読み出し、表示手段17にガス濃度を出力する(ステップホ)。1回の測定が終了した段階で、検出テープ2を1コマ分紙送りして次の測定に移る(ステップヘ)。

【0014】このように、フォトダイオード8からの信号のレベルが基準値に到達するまでサンプリングを継続するから、高い濃度のガスが測定ヘッド4に流入した場合には、検出テープ2が飽和する以前に光学濃度を検出してガスの濃度を検出することができ、また極めて低い濃度のガスが測定ヘッド4に流入している場合には、積分効果を十分に活かすことができるまでサンプリング時間を自動的に延長して検出する。

【0015】

【発明の効果】以上、説明したように本発明においては、ガス検出テープの搬送路に対向して配置された発光手段と受光手段を収容し、被測定環境のガスをガス検出

4

テープに供給するガス導入口を有する測定ヘッドと、測定開始により作動し、また受光手段からの信号が基準値に一致した時点で停止する計時手段と、計時手段の時間を検量データに基づいて被検ガスの濃度に変換する手段とを備えたので、受光手段の信号が基準値に到達するまでサンプリングを継続して、積分効果を十分に活かしてガスを検出することができ、環境中に晒されても変色しない程度の検出感度のテープを用いて極めて低い濃度のアンモニアガスを高い精度で測定することができる。

【図面の簡単な説明】

【図1】本発明のテープ式ガス測定装置の一実施例を示す図である。

【図2】検量データの一実施例を示す線図である。

【図3】同上装置の動作を示すフローチャートである。

【符号の説明】

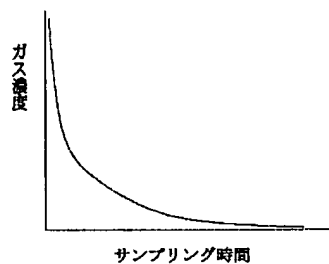
2 ガス検出テープ

7 発光ダイオード

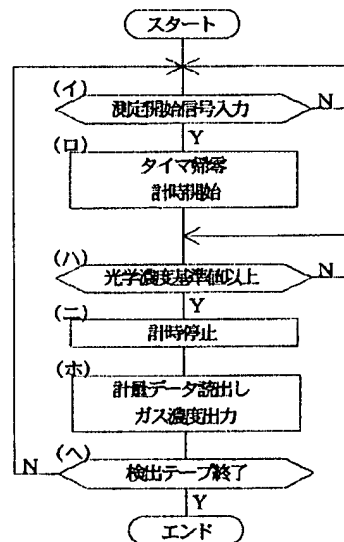
8 フォトダイオード

12 信号処理装置

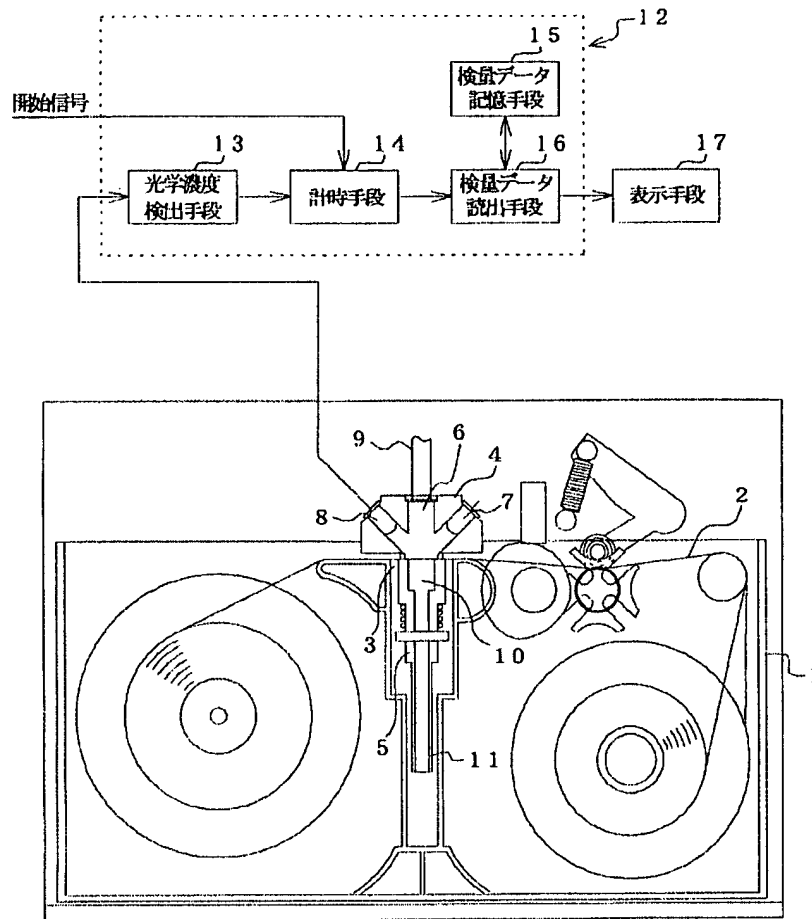
【図2】



【図3】



【図1】



フロントページの続き

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⑬ 発明の名称 水中アンモニア分析装置

① 特 願 昭61-148253

② 出 願 昭61(1986)6月26日

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明 細 書

1. 発明の名称

水中アンモニア分析装置

2. 特許請求の範囲

検水とアルカリ剤とを混合してなる被測定液が連続的に導入され、この被測定液との間に一定容積の気相部が形成されるように構成された測定セルと、この測定セルに前記気相部と接触するように装着されたアンモニア電極と、前記測定セルと連結され、この中の被測定液にアンモニア性窒素濃度が既知の標準溶液を任意の混入率で混入する標準溶液混入機構とを備え、まず、前記標準溶液の混入率を一定にした状態で電極出力をホールドし、次いで電極出力がそのホールド値から一定量だけ変化するように前記混入率を調節し、制御動作による混入率変化から検水中のアンモニア性窒素濃度を求めることを特徴とする水中アンモニア分析装置。

3. 発明の詳細な説明

(発明の属する技術分野)

本発明は水中のアンモニア性窒素(以下、 NH_3 、 $-\text{N}$ と略記する)濃度をオンライン測定する水中アンモニア分析装置に係り、特に、メンテナンスが容易で長期にわたって安定した測定が可能であるとともに、 NH_3 、 $-\text{N}$ の低濃度の測定にも適用し得る水中アンモニア分析装置に関する。

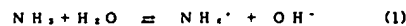
(従来技術とその問題点)

生物学的脱窒プロセスでは、プロセスを監視するために処理水中のアンモニア性窒素(以下、 NH_3 、 $-\text{N}$ と略記する)濃度を測定する必要がある。一方、浄水場では原水の汚染の指標として NH_3 、 $-\text{N}$ の重要性が知られている。このように NH_3 、 $-\text{N}$ 濃度の測定、特にオンラインで長期にわたり自動分析が可能な装置に対する必要性が各方面で指摘されている。

このような要求を満たすために本出願人はガスバージ型アンモニア分析計に関する提案を行い、特願昭59-281422号として特許出願中で

ある。この装置は検水をアルカリ性にして空気でバブリングし、排出ガス中に含まれる NH_3 濃度を測定することを基本原理とし、これに標準添加法を応用したものである。

第3図に前記特許出願に係る分析装置の構成図を示す。第3図において、検水1がサンプリングポンプP1により一定量サンプリングされ、気液接触槽2に注入される。この検水1中にディフューザ3を通して空気が注入され、ばっ気が行われる。P2は空気を供給するためのエアポンプ、4は空気流量を調整するためのバルブ、5は背圧弁である。サンプリング後、アルカリ剤注入機構6により検水1中に水酸化ナトリウムが添加され、検水1のpHを11以上にする。水中の NH_3 、 NH_4^+ は NH_3 および NH_4^+ として存在し、両者の関係は、



と表される。ところが、 $\text{pH} > 11$ では反応はほぼ完全に左側にシフトする。すなわち、 NH_3 、 NH_4^+ は溶解 NH_3 ガスとして存在することになる。こ

の状態で上述のようなばっ気を行うと、上昇気泡中へ水中の NH_3 が放出され、排出ガス中には NH_3 が含まれる。今、水中の NH_3 、 NH_4^+ 濃度を x_1 、排出ガス中の NH_3 、 NH_4^+ 濃度を x_2 とすると、

$$x_2 = \kappa x_1 \quad (2)$$

となる。ここで κ は比例定数である。排ガスはガス透過形 NH_3 電極7が挿入されている電極ハウジング8内を通過して大気中へ放出される。したがって、電極7は x_2 に対応する出力Eを発生する。 x_1 とEとの関係は

$$E = E_0 - S \ln x_2$$

$$S = \frac{RT}{nF} \quad (3)$$

となる。ここでRはガス定数、Tは絶対温度、Fはファラデー定数、nは電極内反応に関与するイオンの電荷数、 E_0 は $x_2 = 1$ におけるEである。この式は一般にネルンストの式と呼ばれている。

式(3)に式(2)を代入すると、

$$E = E_0' - S \ln x_1$$

$$E_0' = E_0 - S \ln \kappa \quad (4)$$

を得る。すなわち、 x_1 とEの関係も式(3)と同様、ネルンストの式で表すことができる。したがって、検水1をアルカリ性にしてばっ気を行い、電力出力が定常値になった時点では式(4)が成り立つ。電極出力は変換器9を介して演算器10に入力されており、演算器10はこの時点の電極出力をホールドする。このホールド値を E_1 とすると、

$$E_1 = E_0' - S \ln x_1 \quad (5)$$

となる。次に標準溶液注入機構11が作動し、既知濃度の NH_3 、 C_2 溶液が一定量注入される。これにより検水1中の NH_3 、 NH_4^+ 濃度は増加し、電極出力も変化する。 NH_3 、 NH_4^+ 濃度変化を Δx_1 、変化後の電力出力を E_2 とすると、

$$E_2 = E_0' - S \ln (x_1 + \Delta x_1) \quad (6)$$

となる。式(6)から式(5)を引くと、

$$\Delta E = E_2 - E_1 = -S \ln \left(1 + \frac{\Delta x_1}{x_1} \right) \quad (7)$$

となる。 ΔE と Δx_1 は既知であり、温度センサ12により電極ハウジング内の温度を測定することによりSも求めることができる。

$$x_1 = \frac{\Delta x_1}{\frac{-\Delta E}{S} - 1} \quad (8)$$

により目的とする x_1 が測定される。測定が終わるとピンチ弁13が開いて検水1が排出され、次の測定に移る。

上述のアンモニア分析計は排ガス中の NH_3 、 NH_4^+ 濃度を測定することにより、水中の NH_3 、 NH_4^+ 濃度を測定するため、検水とセンサが接触せず、電極膜の汚染によるトラブルを防止することができる。また、電極の特性変化、水質変動等による κ の変化は E_0' の変動として現れるが、標準溶液添加方式により E_0' の変化に影響されないで測定が可能である。

以上のように、本出願人にかかる前述の NH_3 分析計は優れた特徴を有するが、反面、以下のような欠点も有している。

まず第1に、式(2)に示したように、 x_2 は x_1 に比例するが、 x_2 は x_1 に対する平衡濃度よりも低い。すなわち、排ガス中の NH_3 分圧は水中の

それよりも低い。このことは NH_3 電極の定置下限付近での測定では、電極を直接、液中に挿入する通常の測定法(水中の NH_3 分圧を測定する)に比較して不利となる。

第2の欠点はばう気による気液接触槽内での発泡の問題である。特に、廃水を対象とした測定では泡が生じ易く、泡が液面上に蓄積して電極ホルダー8内にまで達することがある。発泡は気液接触槽2および配管内部を濡らして汚染する。汚染された部分には NH_3 が吸収されやすいため、 α の変化に対する α の応答が著しく遅れ、ついには測定不能となる。

第3の欠点は標準添加法で精度良く測定を行うためには標準液の添加により NH_3 、 $-\text{N}$ の濃度が2乃至3倍になるように添加量を調節する必要があるということに関連する。すなわち、この方法で信頼性の高い測定を行うためにはあらかじめ検水の NH_3 、 $-\text{N}$ を予測し、その予測値に基づき標準液添加量を設定しなければならない。したがって、 NH_3 、 $-\text{N}$ 濃度の変動が激しい場合には添加

量が最適値からはずれる場合が生じてくる。

(発明の目的)

本発明は上述のような従来のアンモニア分析装置の欠点を解決するためになされたものであって、その目的はメンテナンスが容易で長期にわたり安定な測定が可能であるとともに、低濃度の NH_3 、 $-\text{N}$ 濃度の測定にも適用し得るオンライン用水中アンモニア分析装置を提供することにある。

(発明の要点)

前述の目的を達成するため、本発明によれば、検水とアルカリ剤とを混合してなる被測定液が連続的に導入され、この被測定液との間に一定容積の気相部が形成されるように構成された測定セルと、この測定セルに前記気相部と接触するように装着されたアンモニア電極と、前記測定セルと連結され、この中の被測定液にアンモニア性窒素濃度が既知の標準溶液を任意の混入率で混入する標準溶液混入機構とを備え、まず、前記標準溶液の混入率を一定にした状態で電極出力をホールドし、次いで、電極出力がそのホールド値から一定量だ

け変化するように前記混入率を調節し、制御動作による混入率変化から検水中のアンモニア性窒素濃度を求めることを特徴とする。

上述の先題にかかる水中アンモニア分析計がばう気方式を採用しているのは気液間で NH_3 を平衡状態とするためには長期間を要するという考えに基づいている。すなわち、ばう気方式では排ガス中の NH_3 、 $-\text{N}$ 濃度は水中の NH_3 、 $-\text{N}$ 濃度に対する平衡濃度とはならないが、式(2)の比例関係は成り立つ。平衡関係ではないから、 α は水質、気泡径等により変化するが、標準添加法により α の変動に依存しない形で測定できればよいという考え方である。

これに対して、本発明者らは実験、研究を重ねた結果、 NH_3 の場合、ばう気あるいは機械攪拌等により気液接触効率を高める手段を用いることなく、自由水面における気液接触で容易に気液平衡に達することを見出した。本発明はこのような知見に基づくものであり、以下実施例により詳細に説明する。

(発明の実施例)

第1図は本発明分析装置の構成図であり、第2図は第1図における測定セルの拡大断面図である。第1図中、実線は物質の流れを、破線は信号の流れをそれぞれ表す。検水は採水ポンプP1によりくみ上げられ、分析装置ロック外に設置された採水槽21に導入される。ロック内へは少量の検水が導入され、ピンチ弁V1、チューブポンプP3を通過して測定セル22に入る。その過程で NH_3 、 Cl 標準溶液および NaOH を混入する。 NaOH はアルカリタンク23から定量ポンプP4によりチューブポンプP3の吐出側の検水流路に注入される。注入流量は被測定液のpHが11以上になるように定められる。このようにして検水とアルカリ剤とを混合してなる被測定液が測定セル22に連続的に導入される。

一方、第1図のAは標準溶液混入機構であり、標準溶液が標準溶液タンク24からピンチ弁V2を通過してチューブタンクP3の吸引側流路に入る。

被測定液は第2図示の液流入口31から測定セル

特開昭63-6456 (4)

22内に導入され、液滞留部32を通過して液排出口33から流出する。液滞留部32の被測定液は外部マグネット34との磁気カップリングにより回転する攪拌マグネット35により迅速攪拌される。

また、第2図において、25はアンモニア電極、例えば隔膜式アンモニア電極であって、これは測定セル22内に後述の気相部42と接触するように装着される。例えば、第2図示のようにステンレススチール製の電極ホルダー36に挿入され、フッ素樹脂製のスペーサー37により支持されることにより装着される。電極ホルダー36はバンドヒータ38で加熱されるようになっており、白金測温抵抗体39とこの図には示していない温度調節計を用いて電極ホルダー36の温度が被測定液の温度より高く保たれるようになっている。これはスペーサー内面および電極測定面40の水蒸気が凝縮してNH₃が吸収されるのを防ぐとともに、温度ドリフトによる測定誤差が出ないようにするためである。

この測定セル22の内部には水面41、スペーサー37および電極測定面40により一定容積の気相部42

が形成される。この測定セル22に被測定液を流通すると気相部42のNH₃-N濃度x₀は被測定液中のNH₃-N濃度x₁と平衡状態となる。

すなわち、

$$x_0 = \frac{1}{H} x_1 \quad (9)$$

となる。ここでHはヘンリー定数である。したがって、アンモニア電極25の出力Eは

$$E = E^0 - S \ln x_1 \\ E^0 = E_0 + S \ln H \quad (10)$$

であり、この信号が第1図の演算装置26に入力される。演算装置26はピンチ弁V1とV2を交互に開くためのオンオフ信号を発生し、そのオンオフ比率を調節することにより、標準溶液混入率rを調節する。本実施例では1測定周期を1時間としている。そしてその前半30分が基準化モード、後半30分が測定モードである。基準化モードではrを一定値r₁に固定する。r₁は被測定液のNH₃-N濃度がアンモニア電極の測定限界以上になるように決める。したがって、検水のNH₃-N濃

度が測定限界以上であれば、r₁=0とし、以下ではr₁≠0として議論を進めるが、式中のr₁を零とおくことによりr₁=0の場合も同様に扱えることはもちろんである。

基準化モードでは被測定液のNH₃-N濃度x₁は

$$x_{11} = (1 - r_1) x_0 + r_1 x_2 \\ = x_0 + r_1 (x_2 - x_0) \quad (11)$$

となる。ここでx₀は検水のNH₃-N濃度、x₂は標準溶液のNH₃-N濃度である。

ただし、x₂はx₁に比べて十分高く(x₂ > x₁)を設定するため、

$$x_{11} \approx x_0 + r_1 x_2 \quad (12)$$

となる。そして、電極25は出力

$$E_1 = E^0 - S \ln x_{11} \quad (13)$$

を発生する。基準化モードの終了時点でこの値をホールドし、測定モードに入る。測定モードでは電極出力がE₁から一定量ΔE変化してE₂=E₁+ΔEとなるように標準溶液混入率rを制御する。制御動作が平衡に達した時点でのrをr₂=r₁+

Δrとすると、被測定液のNH₃-N濃度は

$$x_{12} = x_{11} + \Delta r (x_2 - x_0) \\ \approx x_{11} + \Delta r x_2 \quad (14)$$

であり、

$$E_2 = E^0 - S \ln (x_{11} + \Delta r x_2) \quad (15)$$

となる。したがって、式(15)から(13)を引き、

$$\Delta E = -S \ln \left(1 + \frac{\Delta r x_2}{x_{11}} \right) \quad (16)$$

であるから、

$$x_{11} = \frac{\Delta r x_2}{\frac{-\Delta E}{S} - 1} \quad (17)$$

によりx₁₁が求められる。さらに式(12)、

$$x_0 = x_{11} - r_1 x_2 \quad (18)$$

から目的とするx₀が求められる。演算装置26は以上の演算を行い、x₀を測定値として発信する。

(発明の効果)

従来法によるNH₃分析装置がばっ気排ガス中のNH₃-N濃度と水中のNH₃-N濃度の比例関

係、すなわち、式(2)を利用しているのに対して、本発明では気液平衡の式(9)を用いる。したがって、 $x > 1/8$ であるため、同じ x_1 に対して後者の x_2 は前者の x_1 より大きい。さらに本発明では基準化モードにおいて、 $r_1 \neq 0$ とすることにより従来のアンモニア電極では測定不能であった低濃度領域の測定が可能になった。

また、本発明では、ばう気や急速攪拌を用いないため、発泡あるいは飛沫による測定セル内面の汚れも少なく、 NH_3 の吸収による応答の遅れもほとんど生じない。

従来法による NH_3 分析装置と本発明の他の相違点は前者では式(7)、(8)の Δx_1 を一定にして ΔE を求めるのに対し、後者では式(16)、(17)の ΔE を一定にして $\Delta r x_1$ 、すなわち Δx を求める点である。このことによる利点は次のとおりである。

- (1) ΔE を設定すれば $k \frac{-\Delta E}{S}$ は定数として扱えるため指数関数を計算する必要がない。

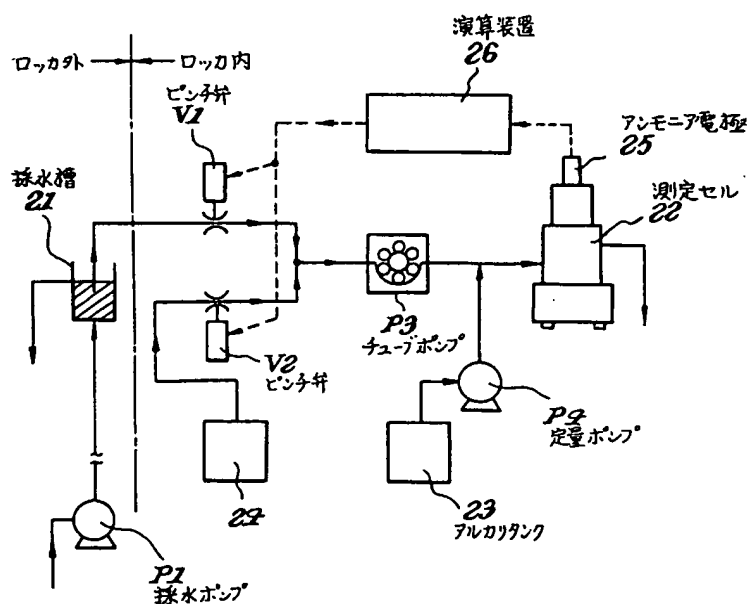
(2) ΔE を決めることにより $\Delta r x_1 / x_{11}$ が決まるため、標準添加法の条件、すなわち、標準液の添加により NH_3 濃度が2乃至3倍変化するという条件を常に満たすように ΔE を設定することができる。

4. 図面の簡単な説明

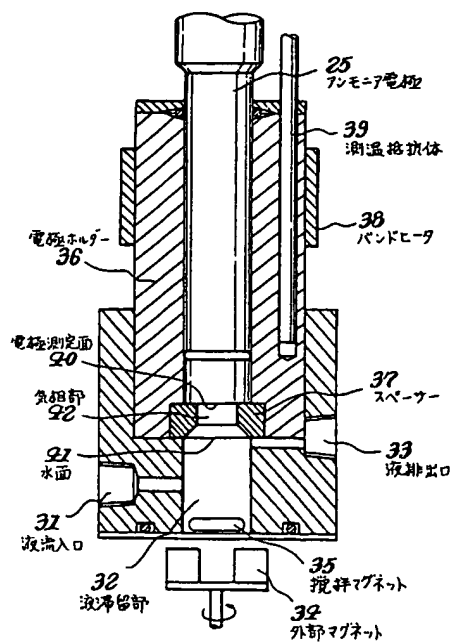
第1図は本発明にかかる装置の一具体例の構成図を示し、第2図は第1図における測定セルの拡大断面図を示し、第3図は従来にかかる装置の構成図を示す。

- 22…測定セル、 23…アルカリタンク、
24…標準溶液タンク、 25…アンモニア電極、
26…演算装置、 31…液流入口、
33…液排出口、 34…外部マグネット、
35…攪拌マグネット、 40…電極測定面、
41…水面、 42…気相部、
A…標準溶液流入機構、 P1…採水ポンプ、
P3…チューブポンプ、 V1、V2…ピンチ弁

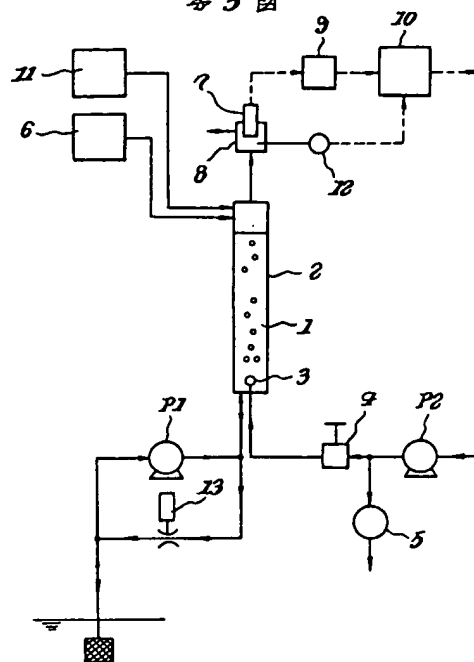
第1図



第 2 図



第 3 図



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(54) 【発明の名称】 血清中ヘリコバクター・ピロリー抗体のウレアーゼ活性阻害による抗体値測定原理

(57) 【要約】 (修正有)

【目的】ヘリコバクター・ピロリー感染者を迅速かつ安価な試薬で診断できる測定原理の提供。

【構成】血清中ヘリコバクター・ピロリー抗体の測定法において、

- 1) 抗原に精製された本菌のウレアーゼを用いること。
- 2) 血清中の抗体によるウレアーゼ活性阻害をアンモニア測定法で定量すること。

1

【特許請求の範囲】

血清中ヘリコバクター・ピロリー抗体の測定法において、

- 1) 抗原に精製された本菌のウレアーゼを用いること。
- 2) 血清中の抗体によるウレアーゼ活性阻害をアンモニア測定法で定量すること。

【発明の詳細な説明】

ヘリコバクター・ピロリーは、胃に感染し、胃炎を惹起する細菌であり、萎縮性胃炎・胃潰瘍・十二指腸潰瘍・胃ガンなどの胃・十二指腸疾患に関与している。本菌感染者の検査方法には、血清学的に血清中の抗体を測定する方法、形態学的に胃生検病理標本あるいは細胞診標本で観察する方法、細菌学的に胃液あるいは胃生検粘膜の細菌培養する方法などがある。現時点の血清学的検査方法は、本菌あるいは本菌のウレアーゼを抗原として血清中の抗体を測定しているが、抗原抗体反応後、別の酵素をラベルした抗ヒト免疫グロブリン兔血清を用いて、抗原に付着したヒト免疫グロブリンとその兔血清と抗原抗体反応後、別の酵素活性で測定している。つまり、酵素免疫吸収法(ELISA)で行なっている。この方法は、別の酵素・兔血清など試薬コストが高く、測定時間も約2時間かかる。私の考案した測定原理は、本菌のウレアーゼに対する抗体を調べる測定原理で、本菌のウレアーゼとアンモニア測定試薬あるいはアンモニア電極があれば簡単に測定できる。すなわち、ヘリコバクター・ピロリー感染者を迅速かつ安価な試薬で診断できる測定原理

2

である。

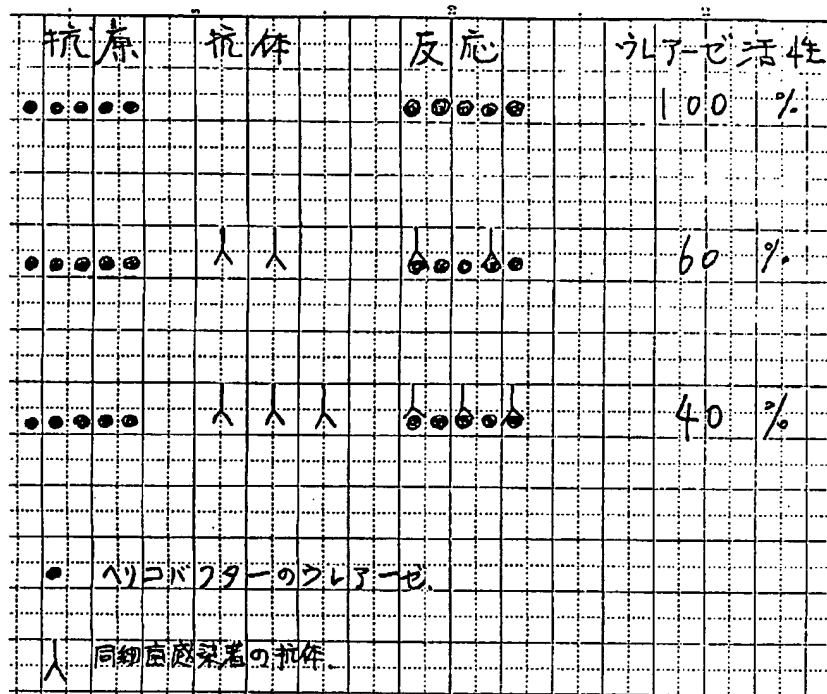
【図面の簡単な説明】

抗原にヘリコバクター・ピロリーから精製したウレアーゼを使用する。抗体はヘリコバクター・ピロリー感染者の血清、この両者を恒温層にて反応させた後、ウレアーゼ活性を測定する。ウレアーゼは尿素を分解して、アンモニアと二酸化炭素にする酵素で、一定量のウレアーゼは一定量のアンモニアを産生する。抗体があれば、ウレアーゼ活性は阻害され、アンモニア量が抗体のないヒトより少ない。

実験

私の実験は、次の順序で行なわれた。本菌から精製したウレアーゼが入手できなかったので、本菌を冷アセトンで固定し、固定後の本菌でウレアーゼ活性を測定したところ、高い活性値が得られた。その活性値を測定にあった一定の値にするように希釈液Aを作り、BとCの二本の試験管に一定量のAと一定量の血清を混和後、一時間恒温槽で反応させる。その後、Bは反応を停止、Cには尿素を添加し、一定時間反応させ、C-Bのアンモニア量からウレアーゼ活性値を換算する。また、Aのウレアーゼ活性値も血清の代わりに水を入れ、同時間反応させて測定した。ヘリコバクター感染者はウレアーゼ活性が50～60%阻害された。この実験のなかで、Bのアンモニア量も阻害を受けており、アンモニア電極があれば、随時活性の低下が測定できるので、尿素添加なしで行なうことができると考えている。

【図1】



【手続補正書】

【提出日】平成5年12月1日

【手続補正2】

【補正対象書類名】明細書

【補正対象項目名】図面の簡単な説明

【補正方法】変更

【補正内容】

【図面の簡単な説明】

【図1】ヘリコバクター・ピロリー抗体測定原理図

【符号の説明】

● ヘリコバクター・ピロリーのウレアーゼ

人 同細菌感染者の抗体

抗原にヘリコバクター・ピロリーから精製したウレアー

ゼを使用する。抗体はヘリコバクター・ピロリー感染者の血清、この両者を恒温層にて反応させた後、ウレアーゼ活性を測定する。ウレアーゼは尿素を分解して、アンモニアと二酸化炭素にする酵素で、一定量のウレアーゼは一定量のアンモニアを産生する。抗体があれば、ウレアーゼ活性は阻害され、アンモニア量が抗体のないヒトより少ない。

【手続補正3】

【補正対象書類名】図面

【補正対象項目名】全面

【補正方法】変更

【補正内容】

【図1】

(4)

特開平7-5175

図1

抗原	抗体	反応	ウレデ活性
●●●●●		●●●●●	100 %
●●●●●	人 人	●●●●●	60 %
●●●●●	人 人 人	●●●●●	40 %

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33/50	T			
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A 6 1 K 49/00	A			

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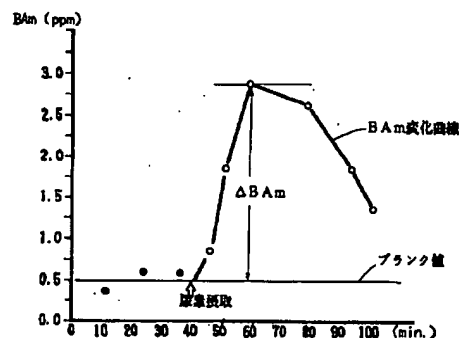
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(54) 【発明の名称】 ウレアーゼ活性を有する微生物の感染判定方法

(57) 【要約】 (修正有)

【目的】 消化器系に感染するウレアーゼ活性を有する微生物の存在を判定する場合に、無侵襲で特殊な試薬や装置を必要とせず、しかも迅速に測定できる方法を提供する。

【構成】 空腹時の被検者に標識を付していない尿素を経口投与し、所定時間後に呼気中のアンモニアガス濃度を測定することによって、ウレアーゼ活性を有する微生物、特にヘリコバクター・ピロリの感染の有無を判定する。



【特許請求の範囲】

【請求項1】 空腹時の被検者に尿素を経口的に服用させ、所定時間経過後に呼気中のアンモニア濃度を測定することを特徴とする、ウレアーゼ活性を有する微生物の感染判定方法。

【請求項2】 尿素負荷前の呼気中アンモニアレベルをブランク値とし、尿素負荷後のアンモニア濃度と比較するものである請求項1記載のウレアーゼ活性を有する微生物の感染判定方法。

【請求項3】 呼気中のアンモニア濃度を、ガス検知管や発色試験紙、或いは分離カラムと高感度な検出器を組み合わせた装置を用いて測定するものである請求項1記載のウレアーゼ活性を有する微生物の感染判定方法。

【発明の詳細な説明】

【0001】

【産業上の利用分野】本発明は、消化器系に感染するウレアーゼ活性を有する微生物の存在を判定する新規な方法に係わり、特に胃粘膜に感染するヘリコバクター・ピロリの感染の有無を、呼気中のアンモニアガス濃度を測定することにより判定するものに関する。

【0002】

【従来の技術】ヘリコバクター・ピロリは、慢性胃炎患者の胃前庭部生検組織より分離同定されたらせん状の細菌であり、消化性潰瘍においても高率に検出される。そこで特に欧米では、ヘリコバクター・ピロリが、胃炎及び消化性潰瘍の少なくとも重要な因子の一つであると言う認識が広くなされている。また最近では胃癌との関連も指摘され、本菌に体する研究が勢力的になされている。

【0003】上記のような認識は、ヘリコバクター・ピロリが極めて高いウレアーゼ活性（尿素分解能）を有しており、これが胃液中に1 mM前後含まれている尿素を分解して高濃度のアンモニアを発生させ、胃上皮細胞に障害を与えんと言ふ考えに立脚している。また、アンモニアガスのアルカリ性が胃液中の塩酸を中和し、ヘリコバクター・ピロリの周辺にミクロの中性環境を作り上げていることに立脚している。また、ビスマス製剤等の抗菌剤投与でヘリコバクター・ピロリを除菌すると潰瘍再発率が低下することも、上記因子説の有力な左証となっている。

【0004】尚、一般に細菌感染を確認するためには、試料から細菌を検出してその細菌の生化学的性状や形態学的特徴などから菌を同定することが原則である。ヘリコバクター・ピロリの感染を診断する場合にも、胃粘膜からヘリコバクター・ピロリを分離培養して菌を同定する必要がある。しかし、微好気性菌であるヘリコバクター・ピロリを分離同定するには特殊な培地が必要であるし、発育が遅いため日数もかかる。そこで、臨床分野においては培養法の欠点を補うべく簡便な検査方法が幾つか利用されている。1つは①組織学的検出法であり、他

の1つはヘリコバクター・ピロリの特異なウレアーゼ活性を利用するものである。

【0005】前者(①)は、内視鏡を用いて胃粘膜組織を採取し、その切片を染色して顕微鏡により菌を同定するものである。一方後者としては、②抗体測定法、③迅速ウレアーゼテスト、④フェノールレッド色素内視鏡検査法、⑤呼気中 $^{13}\text{C}\text{O}_2$ 又は $^{14}\text{C}\text{O}_2$ 測定法、及び⑥ ^{15}N -尿素の経口投与による尿検査が現在行われている。

【0006】②の抗体測定法は、ヘリコバクター・ピロリの菌体或いは菌体抽出物を抗原として用いる抗原-抗体反応により感染の程度を判定するものである。また、③の迅速ウレアーゼテストは、内視鏡検査時に得られた生検粘膜組織を尿素とpH指示薬を含んだ試薬に入れ、pH指示薬の色の変化を肉眼で観察してヘリコバクター・ピロリの存在を判定する。④のフェノールレッド色素内視鏡検査法は、前日にオメプラゾール投与するなどの前処置を施した後、0.5 Mの尿素を添加した0.05%フェノールレッド溶液を経内視鏡的に胃内に散布し、変色程度からヘリコバクター・ピロリの陽性率を判断するものである。

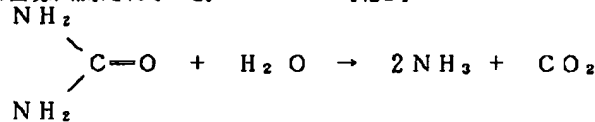
【0007】また、⑤の呼気中 $^{13}\text{C}\text{O}_2$ 又は $^{14}\text{C}\text{O}_2$ 測定法は、空腹時に被検者に標識尿素(^{13}C 又は ^{14}C -尿素)を経口的に服用させ、ウレアーゼ活性によりアンモニアと二酸化炭素($^{13}\text{C}\text{O}_2$ 又は $^{14}\text{C}\text{O}_2$)に分解させる。発生した二酸化炭素は消化管から吸収され、血液を介して肺から呼気中に排出される。そこで、呼気中に含まれる $^{13}\text{C}\text{O}_2$ 又は $^{14}\text{C}\text{O}_2$ を計測し、その量からヘリコバクター・ピロリの感染を判定する。 $^{13}\text{C}\text{O}_2$ の場合は質量分析により、 $^{14}\text{C}\text{O}_2$ の場合は放射線量を測定して判定する。⑥の ^{15}N -尿素の経口投与の場合、方法や原理は呼気検査と同様である。尿素が分解されて発生するアンモニアが消化管より吸収され、再び二要素に合成されて尿中に排出される尿素中の標識された窒素原子を測定して、ヘリコバクター・ピロリの感染を判定するものである。

【0008】

【発明が解決しようとする課題】ところがこれらの従来方法は、内視鏡が必要で被検者に苦痛を与える(①、③、④)とか、血清が必要で同じく被検者に苦痛を与える(②)とか、大形で高価な装置と専門オペレータを必要とする(②、⑤、⑥)とか、専門試薬や培地等の消耗品を必要とする(②、④、⑤、⑥)とか、測定結果がでるまで時間がかかる(①、②、⑤)など、多くの点で問題がある。尚、⑤の呼気中 $^{13}\text{C}\text{O}_2$ 又は $^{14}\text{C}\text{O}_2$ 測定法及び⑥の ^{15}N -尿素の経口投与の場合、他の方法に比べて胃全体の感染を評価できるし患者に苦痛を与えない(無侵襲性)と言う大きな特徴を有するが、1 g当たり数万円もする標識尿素を使用するのが大きな難点である。しかも、ヘリコバクター・ピロリの除菌のための治療にはこれを数回以上繰り返さなくてはならず、患者に

取って精神的、肉体的或いは金銭的苦痛は極めて大きなものとなる。

【0009】従って、ヘリコバクター・ピロリの除菌のための治療の必要性が高まっている現在においても、胃炎や胃潰瘍、十二指腸潰瘍或いは胃癌の患者の内の極く少数しかこれらの検査を受けていないのが実情である。そこで、ヘリコバクター・ピロリの感染の判定や治療のために、より簡便で迅速に測定でき、しかも無侵襲性で且つ低コストな検査方法の出現が希求されていた。



で示すようにウレアーゼによりアンモニアと炭酸ガスに分解される。生成したアンモニアは、消化管壁を通過して血中

【化1】に移行する。血中に入ったアンモニアガスの一部は、肺を介して呼気中に排出される。本発明では、ウレアーゼ活性のある細菌（主としてヘリコバクター・ピロリ）の存在を、尿素から発生する呼気ガス中に含まれるアンモニアガスのレベルを知ることにより判定しようとするものである。

*【0010】

【課題を解決するための手段】そこで本発明者は、上記諸問題を解決するために鋭意研究した結果本発明を完成させたものである。そしてその特徴とするところは、被検者に尿素を摂取させ、ウレアーゼで分解されて呼気中に排出されるアンモニアガスを高感度な測定手段で測定して感染の有無を判定するものである。

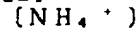
【0011】即ち、経口的に摂取した尿素は

【化1】

※ロリ）の存在を、尿素から発生する呼気ガス中に含まれるアンモニアガスのレベルを知ることにより判定しようとするものである。

【0012】ところで、アンモニアは胃液或いは血液中で、そのときのpHによって存在形は異なり、

【化2】



、図4に示すようにアンモニアとアンモニウムイオンの比率がpHに大きく変化する。血液（血漿）のpHの正常値は7.4近傍であるから、

【化2】血中NH₃（フリーアンモニア）は、数%の存在比率を持っている。一方、そのフリーNH₃は、呼気中には肺を介して移行するがNH₃の拡散能は非常に高く、O₂の3万倍、CO₂の1,500倍と言われている。即ち、NH₃は両者に比較してはるかに肺胞膜を透過しやすく、血中アンモニア変化と肺胞アンモニア変化はほぼ同期すると見て差支えない。

【0013】本発明のポイントは、呼気中に現出するアンモニアを正確に測定することにある。そして、そのプロトコルは次の通りである。①一晩の絶食のあと（空腹時）に、呼気中アンモニア（BAm）を測定し、これをブランク値とする。数回測定の平均値を取ることが好ましい。②次に、少量の尿素（例えば体重1kg当たり3mg前後）を水に解かして経口摂取し、所定時間経過後に同様に呼気中アンモニア（Breath ammonia: BAm）を測定する。通常、摂取後10〜30分程度後に呼気中のアンモニアガスのピークが現れるので、摂取後5〜10分間隔で1時間程度後まで測定する。③測定結果を図3のごとくプロットし、ヘリコバクター・ピロリの感染の有無を判定する。

【0014】但し、アンモニアガスの濃度は数ppm単位である。従って、その測定は極めて高感度、高精度な測★

★定手段が必要となる。ガス検知管、アンモニア測定用発色試験紙、ガスクロマトグラフィーなどが好適に用いられる。ガス検知管の場合は、風船に採取した被検者の呼気を、公知のアンモニア用ガス検知管で測定する。この場合、風船を体温程度（例えば40℃）の恒温層に入れておくと、アンモニアガスを吸着している風船内壁面の水滴を気化できるため、測定誤差が生じない。

【0015】或いは図1に示すように、アンモニアガスと化学反応を起こして呈色する発色試験紙を用いる方法もある。この装置は、発色試験紙1の両側を呼気採取管2と吸引管3で挟み、吸引ポンプ4で呼気Bを計量しつつ吸引し、アンモニアガスによって発色した程度を光反射率計5で測定するものである。符号6は呼気採取マスク（マウスピースでもよい）。尚、発色試験紙の代わりに発色剤（ゲルディスク）を用い、透過光測定器と組合せる方法も考えられる。

【0016】更に、図2に示すように分離カラム7とアンモニアガスを特異的に検出できる検出器8とを組合せた装置も使用できる。検出器としては、IMS（Ion Mobility Spectrometer：イオン移動度スペクトル検出器）、ECD（Electron Capture Detector：電子捕獲型イオン検出器）或いはPID（Photo Ionization Detector：光イオン検出器）が使用可能であるが、中でも放射線を使用せずしかも小型軽量化が可能なPIDが最も好ましい。尚、図中符号9はキャリアガス（PIDの

場合は空気)ポンベ、符号10と符号11は三方電磁バルブ、12はサンプリング定量部、13は呼吸吸引用ポンプである。またこの装置は、検出器8から出力される測定信号を受け入れて演算処理し、予め記憶させている検量線からアンモニアガス濃度を算出し、その結果を記憶したり表示装置に出力する演算処理部を備えている。

尚、これらの装置で使用する呼吸採取管2は、水滴着防止の観点から内壁面を体温程度以上に加温できるタイプのものが好ましい。

【0017】上記した装置の中で、ガス検知管は初期コストは最も安いが、測定は他の装置に比べて手間がかかる。また、発色試験紙による測定は、試験紙の感度にもよるが呼吸を数分程度吸引する必要があり、やや時間がかかる。これに対し、分離カラムと検出器特にPIDを用いたものにあっては、被検者は一息吹き込むだけで済むので極めて簡便であり、しかも高精度な結果が得られるものである。

【0018】尚、本発明で使用する尿素は、従来方法とは異なり標識していない尿素であるため、試薬代は極めて安価ですむ。最も、標識した尿素が一部混入していても、測定には何ら差支えない。

【0019】

【実施例】次に、本発明を実施例により詳細に説明する。図3のグラフは、図2に示す分離カラム7とアンモニアガスの特異的に検出できる検出器(PID)8とを組合せた本発明者自作の装置を用い、ヘリコバクター・ピロリ陽性者の呼吸中に含まれるアンモニアガス(BAm)を測定したBAm変化曲線(n=12)を示すグラフである。測定条件は以下の通りである。まず、各被検者の空腹安静時の呼吸を測定する。呼吸のサンプル量は0.5mlであり、呼吸採取には約3〜8秒程度かかった。また、1回の測定に要する時間は約2.5分程度であった。そして各々3回ずつ測定したところ、その平均値は約0.5ppmとなった。これをブランク値とした。尚、この値は、胃液中に含まれる尿素に由来するもので、個人差が見られる。

【0020】次いで、各人に200mgの尿素(体重1kg当たり約3mg)を、30mlの蒸留水に溶解して経口摂取させた。摂取から5分後及びその後10分間隔で上記と同じ条件で計6回呼吸中のアンモニア濃度を測定した。その平均をプロットしたのが図3である。図3から、判るように、尿素摂取後約20分でアンモニアガス濃度のピークが見られた。尚、図示は省略するが、陰性者の場合には尿素を摂取した後40分間程度はアンモニアガス濃度に殆ど変化がみられない。しかし、その後次第に増加し、約2時間後にアンモニアガス濃度のピークが現出した。これは、胃の中では尿素が殆ど分解されなかったことを示す。尚、2時間後のピークは、腸に棲息するプロテウスや緑膿菌等のウレアーゼ活性に起因するものと思われる。

【0021】従って、ヘリコバクター・ピロリの感染の有無を判定する被検者について、図3のようにBAm変化曲線を描き、その差(ΔBAm)が大きければ感染しており、その差が小さければ感染していない、或いは除菌が成功しつつあるということが判定される。

【0022】

【発明の効果】以上詳述したように、本発明は空腹時の被検者に尿素を経口的に服用させ、所定時間経過後に呼吸中に含まれるアンモニアガスの濃度を測定することにより、ウレアーゼ活性を有する微生物特にヘリコバクター・ピロリの感染の有無或いは程度を判定するものである。

【0023】従って、以下に述べるような種々の利点がある。

① 内視鏡の使用や採血を伴わない無侵襲的な測定方法であるので、被検者に精神的、肉体的な苦痛を与えない。

② 使用する試薬は普通の尿素のみであるため試薬代が極めて安価ですむ、またアンモニアガスの測定にも大形で高価な装置や専門オペレータを必要としないので、測定コストが極めて安価である。

③ 呼吸の分析に要する時間は、1回あたり2〜3分程度であり極めて短くて済む。ただ、尿素の服用からアンモニアガス排出のピークまで約20分かかるので、感染の有無判定は30分程度もあればおおよそ見当が付く。

④ 従って、ヘリコバクター・ピロリの除菌のための治療のために度々ウレアーゼ活性の測定を行っても、患者には殆ど精神的、肉体的或いは金銭的な苦痛を与えず、大量に存在する胃炎や胃潰瘍、十二指腸潰瘍或いは胃癌の患者にとって大きな福音となるものである。

【図面の簡単な説明】

【図1】発色試験紙を用いるアンモニアガス濃度測定装置の一例を示す模式図である。

【図2】分離カラムと検出器とを組み合わせたアンモニアガス測定装置の一例を示す模式図である。

【図3】ヘリコバクター・ピロリ陽性者の呼吸中に含まれるアンモニアガス(BAm)変化曲線を示すグラフである。

【図4】pHによる NH_4^+ イオンと NH_3 との比率の変化を示すグラフである。

【符号の説明】

- 1 発色試験紙
- 2 呼吸採取管
- 3 吸引管
- 4 吸引ポンプ
- 5 光反射率計
- 6 呼吸採取マスク
- 7 分離カラム
- 8 検出器
- 9 キャリアガスポンベ

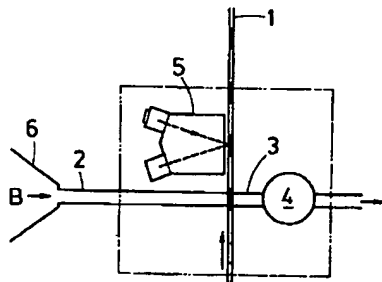
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特開平8-145991

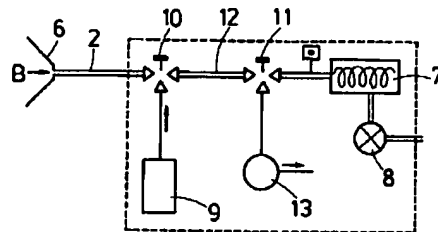
- 7
10 三方電磁バルブ
11 三方電磁バルブ
12 サンプル定量部

- 8
13 呼吸吸引用ポンプ
B 呼吸

【図1】

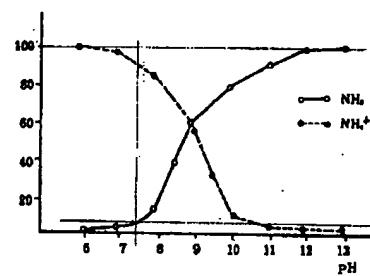
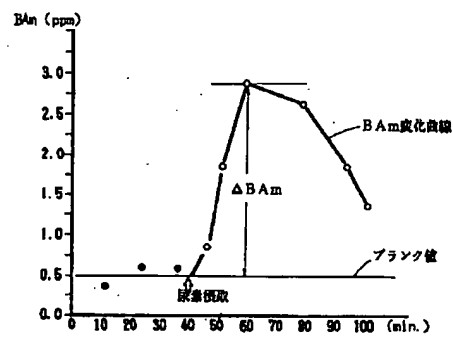


【図2】



【図4】

【図3】



27. RU 2069699C. Diagnosis of chronic gastritis associated with Helicobacter pylori - by determination of presence of ammonia in gastric secretion, yellow colouration indicating chronic gastritis. GODUN, B S, et al. C12Q001/10.



(19) **RU** ⁽¹¹⁾ **2 069 699** ⁽¹³⁾ **C1**

(51) МПК⁶ **C 12 Q 1/10**

РОССИЙСКОЕ АГЕНТСТВО
ПО ПАТЕНТАМ И ТОВАРНЫМ ЗНАКАМ

(12) ОПИСАНИЕ ИЗОБРЕТЕНИЯ К ПАТЕНТУ РОССИЙСКОЙ ФЕДЕРАЦИИ

(21), (22) Заявка: 5020393/14, 27.12.1991

(46) Дата публикации: 27.11.1996

(56) Ссылки: Marshall B. et al Rapid urease test
in the management of Campylobacter pyloridis
- associated gastritis. Amer. J. Gastroent.-
1987, - v. 82, N 3, p. 200 - 210.

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**(54) СПОСОБ ДИАГНОСТИКИ ХРОНИЧЕСКОГО ГАСТРИТА, АССОЦИИРОВАННОГО С HELICOBACTER
PYLORI**

(57) Реферат:

Использование: медицина, в частности
микробиология; может применяться в
гастроэнтерологии. Сущность изобретения: у
больного берут стерильным катетером
слизистый секрет желудка со всей
поверхности антрального и пилорического
отделов, помещают его в стерильную
пробирку и смешивают с реактивом Несслера.

Положительный результат фиксируется
практически мгновенно по окрашиванию
смеси в желтый цвет и/или выпадению
осадка. Положительная реакция
свидетельствует о связи хронического
гастрита у данного больного с Helicobacter
pylori. Способ позволяет повысить точность
диагностики и ускорить ее. 2 табл.

RU 2 069 699 C1

RU 2 069 699 C1



(19) **RU** ⁽¹¹⁾ **2 069 699** ⁽¹³⁾ **C1**

(51) Int. Cl.⁶ **C 12 Q 1/10**

RUSSIAN AGENCY
FOR PATENTS AND TRADEMARKS

(12) **ABSTRACT OF INVENTION**

(21), (22) Application: 5020393/14, 27.12.1991

(46) Date of publication: 27.11.1996

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(73) Proprietor:

Nizhevich Aleksandr Al'bertovich,
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(54) **METHOD FOR DIAGNOSIS OF CHRONIC GASTRITIS ASSOCIATED WITH HELICOBACTER PYLORI**

(57) Abstract:

FIELD: medicine, microbiology, gastroenterology. SUBSTANCE: stomach mucous secret sample is taken in patient with sterile catheter from total surface of antral and pylorus region, placed it in sterile tube and mixed with Nessler reagent.

Positive result is recorded by practically momentary mixture staining with yellow color and/or deposit precipitation. Positive reaction proves association of chronic gastritis in patient with Helicobacter pylori. EFFECT: enhanced precision and accelerated diagnosis. 1 tbl

RU 2 069 699 C1

RU 2 069 699 C1

Изобретение относится к медицинской микробиологии и может быть использовано в гастроэнтерологии.

Известны способы диагностики хронического гастрита ассоциированного с *Helicobacter pylori*: бактериологический, дыхательный, гистологический, иммунологический, ферментативно-селективный.

Из известных способов наиболее близким к изобретению по совокупности признаков является ферментативно-селективный или С1О-тест [1]

Указанный способ диагностики хронического гастрита основан на выявлении *Helicobacter pylori* и выполняется следующим образом: осуществляют забор биоматериала кусочка слизистой оболочки желудка биоптата, смешивают с растворами индикатора фенол-рот и мочевины и инкубируют в термостате при 37°C. Под воздействием продукта жизнедеятельности *Helicobacter pylori* - уреазы происходит расщепление мочевины, в результате чего образующийся аммиак защелачивает среду и индикатор окрашивает раствор в красный цвет. Продолжительность получения результатов реакции зависит от количества бактерий и биоптата и при невысокой степени обсемененности биоптата продолжительность анализа составляет 24 ч, которые необходимы для накопления в среде порогового количества уреазы [2]

Кроме того, вследствие очаговости расселения *H. pylori* на слизистой оболочке антрального отдела желудка, биоптат может не содержать искомый микроорганизм, находящийся на соседних участках, что приводит к ложноотрицательным результатам.

Таким образом, известный способ диагностики достаточно длителен и в части случаев сопровождается ложноотрицательными реакциями.

Цель изобретения ускорение диагностики и повышение точности способа.

Цель достигается тем, что у больного берут слизистый секрет желудка, смешивают его с реактивом Несслера и по окрашиванию смеси в желтый цвет и/или выпадению из нее осадка определяют наличие хеликобактерий.

Общими для предлагаемого объекта изобретения и прототипа существенными признаками являются: забор биоматериала желудка, смешивание биоматериала с индикатором и постановка диагноза по появлению окрашивания смеси.

Отличительными признаками предлагаемого способа являются использование в качестве биоматериала слизистого секрета желудка, смешивание его с реактивом Несслера и постановка диагноза по окрашиванию смеси в желтый цвет и/или выпадению осадка.

Поскольку взятие биоматериала в виде слизистого секрета желудка осуществляется со всей поверхности антрального и пилорического отделов, исключается возможность получения ложноотрицательного результата.

Продолжительность анализа по способу-прототипу зависит от количества хеликобактерий и составляет от 30 мин до 24 ч, что связано с необходимостью инкубирования микроорганизма для

накопления в среде порогового количества уреазы, способного изменить цвет среды. В предлагаемом способе нет необходимости в инкубировании, так как использование реактива Несслера позволяет определить даже небольшие количества аммиака в среде (0,25 мкг) - [3] поэтому положительный результат фиксируется практически мгновенно.

Приведенная совокупность существенных признаков в литературе не описана. Не обнаружено также сведений о применении реактива Несслера для выявления микроорганизмов при диагностике заболеваний.

Проведенный анализ позволяет сделать вывод о соответствии предлагаемого способа критериям "новизна" и "изобретательский уровень".

Способ иллюстрируется следующими примерами.

Пример 1. Больная Г. 8 лет, поступила в клинику с жалобами на боли в эпигастриальной области, возникающие сразу после приема пищи, слабость, утомляемость. Из анамнеза известно, что такие боли отмечаются почти ежедневно в течение двух лет. Девочка неоднократно получала курсы традиционной терапии: витамин U, холензим, гастротарм, фестал, алмагель без значительного улучшения состояния. Проведено обследование обычными методами: общие анализы крови и мочи, осмотр. Проведена фиброгастроскопия со взятием слизистого секрета желудка стерильным катетером при помощи электроотсоса в количестве 0,3 мл. Полученный секрет смешивают в стерильной пробирке с 1 каплей (из офтальмологической пипетки) реактива Несслера. В результате получено окрашивание смеси в желтый цвет (положительный результат). Эндоскопически: явления антропилоporического гипертрофического гастрита. Окончательный диагноз: хронический гастрит, ассоциированный с *H. pylori*, фаза обострения.

Пример 2. Больной X, 14 лет, обратился с жалобами на боли в эпигастриальной области, возникающие натощак, до приема пищи; иногда боли появлялись ночью; запоры до двух дней, утомляемость, слабость. Из анамнеза известно, что такие боли имеют место весной и осенью в течение 3 лет. При обращении к врачу назначалось лечение: диетотерапия, спазмолитики, витаминотерапия, альмагель, калмагин, фестал.

Улучшение состояния отмечалось незначительное и кратковременное. Проведено обследование обычными методами: общий анализ крови, общий анализ мочи, осмотр. Проведена фиброгастроскопия со взятием слизистого секрета желудка стерильным катетером при помощи электроотсоса в количестве 0,4 мл. Полученный секрет смешивают в стерильной пробирке с 1 каплей (из офтальмологической пипетки) реактива Несслера. В результате получен желто-коричневый осадок из смеси (резко положительный результат). Эндоскопически: явления эрозивного антропилоporического гастрита. Окончательный диагноз: хронический гастрит, ассоциированный с *H. pylori*, фаза обострения.

При постановке окончательного диагноза

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назначена антибактериальная терапия (де-нол, трихопол, оксациллин в возрастных дозировках) и диетотерапия в течение месяца. Контрольная фиброгастроскопия, проведенная после окончания курса лечения, показала исчезновение признаков гастрита: визуально - нормализация состояния слизистой оболочки желудка; при исследовании секрета желудка по предлагаемому способу отмечена отрицательная реакция, что соответствует состоянию здорового человека.

Сравнительные данные по точности и продолжительности способа приведены в табл. 1 и 2. Таким образом, как видно из таблиц и приведенных примеров, предлагаемый способ диагностики хронического гастрита позволяет по сравнению с прототипом повысить точность и скорость диагностики. Способ атрауматичен и прост в исполнении.

Использованные источники информации

1. Marshall B. Warren J. et al. Rapid urease test in the management of *Campylobacter pyloridis* associated gastritis

"Amer.J.Gastroent." 1987, Vol. 82, N 3, p.200-210.

2. П. Я. Григорьев, В.З.Арба, В.А.Исаков, А.В.Степанов Некоторые особенности эндоскопической диагностики язвенной болезни и хронического гастрита, ассоциированных с *Campylobacter pyloridis* Тер.архив, 1989, т.61, N 11, с.65-69.

3. В.Д.Пономарев "Аналитическая химия", М. Высшая школа, 1982, часть 1, с.205-206.

Формула изобретения:

Способ диагностики хронического гастрита, ассоциированного с *Helicobacter pylori*, включающий взятые биоматериалы желудка, смешивание его с индикатором с последующей оценкой характера окраски смеси, отличающийся тем, что в качестве биоматериала используют слизистый секрет желудка, в котором определяют с помощью индикатора наличие аммиака и по окрашиванию смеси в желтый цвет и/или выпадению из нее осадка диагностируют хронический гастрит ассоциированный с *Helicobacter pylori*.

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Таблица 1

Группа	C10 тест		Гистология		Люминесцентная микроскопия		Тест с реактивом Нессл.	
	+	-	+	-	+	-	+	-
Больные хронич. гастритом, ассоциированным с H pylori (n = 46)	40	6	46	-	46	-	46	-
Практически здоровые (n = 20)	-	20	-	20	-	20	-	20

+ (положительная реакция)

- (отрицательная реакция)

n - количество наблюдений

5

Таблица 2

Тесты	C10 - тест (n = 46)	Тест с реактивом Несслера (n = 46)
Время появления + результата		
Сразу	-	46
Через 30'	15	
Через 3 часа	33 (15 + 18)	
Через 24 часа	40 (33 + 7)	

RU 2069699 C1

RU 2069699 C1

387522 **IMAGE Available
Derwent Accession: 2006-087414
UTILITY

One-step enzymatic and amine detection technique

Inventor: Song, Xuedong, Roswell, GA, US
Boga, RameshBabu, Roswell, GA, US
Chidebelu-Eze, Chibueze Obi, Atlanta, GA, US

Assignee: Kimberly-Clark Worldwide, Inc., (02)

Correspondence Address: Dority & Manning, P.A., P.O. Box 1449, Greenville, SC, 29601, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060003336	A1	20060105	US 2004881010	20040630

Fulltext Word Count: 17122

Abstract:

...amine within a test sample is provided. For example, in one embodiment, a diagnostic test kit is employed that utilizes reactive complexes that each includes a substrate joined (e.g., covalently...

...the reactive complexes, enzymes may cleave the substrate and release the reporter. Moreover, the test kit may also employ a chemichromic dye, i.e., a dye that exhibits a detectable color...

Summary of the Invention:

...0005] In accordance with one embodiment of the present invention, a diagnostic test kit for detecting an amine, enzyme, or enzyme inhibitor within a test sample (e.g., vaginal fluid) is disclosed. The kit comprises a plurality of reactive complexes that each comprises a substrate joined to a reporter...

...a separation species. The substrate is cleavable by an enzyme to release the reporter. The kit further comprises a chromatographic medium that defines a first enzyme detection zone within which an...

Description of the Invention:

...of one embodiment of an assay device that may be used in the diagnostic test kit of the present invention...or an amine within a test sample. For example, in one embodiment, a diagnostic test kit is employed that utilizes reactive complexes that each includes a substrate joined (e.g., covalently...

...the reactive complexes, enzymes may cleave the substrate and release the reporter. Moreover, the test kit may also employ a chemichromic dye, i.e., a dye that exhibits a detectable color...separation techniques, magnetic separation techniques, etc. In one particular embodiment, for example, the diagnostic test kit contains an assay device that employs a chromatographic medium for separating unreacted complexes from released reduce the costs of the resulting diagnostic test kit for many consumer applications, including those in which a disposable kit is desired. Further, the use of a chromatographic medium also provides for a mechanism in...

...may be simultaneously tested in a single step. That is, a user may use the kit to test a single sample for an enzyme (or inhibitor) and/or amine...0072] Another example of a suitable triarylmethane dye is alpha

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VSP

- naphtholbenzein and analogs thereof. Alpha - naphtholbenzein turns from an orange/red color to a gray/black color upon reaction with an amine. Alpha - naphtholbenzein contains a hydroxyl-substituted naphthyl group, a carbonyl-substituted naphthyl group, and a phenyl group. Specifically, the structure of alpha - naphtholbenzein is ...pale yellow color to a blue/green color upon reaction with an amine. Similar to alpha - naphtholbenzein, naphthochrome green contains a hydroxyl-substituted naphthyl group, a carbonyl-substituted naphthyl group, and a... Besides diagnosing one or more types of infection in vaginal fluid, the method and diagnostic kit of the present invention may be used in any other application in which the detection... membrane (downstream from the first enzyme detection zone) to form a second enzyme detection zone. Alpha - naphtholbenzein (ANB) (5 milligrams per milliliter, Sigma-Aldrich Chemical Co., Inc.) was also striped onto the ...

Exemplary or Independent Claim(s):

1. A diagnostic kit for detecting an amine, enzyme, or an enzyme inhibitor within a test sample, the kit comprising:
a plurality of reactive complexes that each comprises a substrate joined to a reporter...

- ...19. A diagnostic kit for detecting an amine or a hydrolytic enzyme within a test sample, the kit comprising:
a plurality of reactive complexes that each comprises a substrate joined to a reporter...

Non-exemplary or Dependent Claim(s):

2. A diagnostic test kit as defined in claim 1, wherein the enzyme is a protease or peptidase...
- ...3. A diagnostic test kit as defined in claim 1, wherein said substrate is a protein, glycoprotein, peptide, nucleic acid...
- ...4. A diagnostic test kit as defined in claim 1, wherein said substrate is casein, albumin, hemoglobin, myoglobin, keratin, gelatin ...
- ...5. A diagnostic test kit as defined in claim 1, wherein said reporter comprises a detectable substance that is capable6. A diagnostic test kit as defined in claim 1, wherein said reporter comprises a specific binding member...
- ...7. A diagnostic test kit as defined in claim 6, further comprising probes conjugated with a specific binding member, said...
- ...8. A diagnostic test kit as defined in claim 1, wherein said separation species is a specific binding member...
- ...9. A diagnostic test kit as defined in claim 8, wherein a receptive material is immobilized within said first enzyme10. A diagnostic test kit as defined in claim 1, wherein said separation species is a magnetic particle...
- ...11. A diagnostic test kit as defined in claim 10, further comprising a magnetic device positioned adjacent to said chromatographic...
- ...12. A diagnostic test kit as defined in claim 1, wherein said chromatographic medium further comprises a second enzyme detection...
- ...13. A diagnostic test kit as defined in claim 12, wherein a second

receptive material is immobilized within said second14. A diagnostic test kit as defined in claim 12, wherein a second receptive material is immobilized within said second...

- ...15. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is an arylmethane...
- ...16. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is a triarylmethane having the following...17. A diagnostic test kit as defined in claim 1, wherein said chemichromic dye is a diarylmethane...
- ...18. A diagnostic test kit as defined in claim 1, wherein said amine detection zone is positioned downstream from said...
- ...20. A diagnostic test kit as defined in claim 19, wherein said reporter comprises a detectable substance that is capable...
- ...21. A diagnostic test kit as defined in claim ...22. A diagnostic test kit as defined in claim 21, further comprising probes conjugated with a specific binding member, said...
- ...23. A diagnostic test kit as defined in claim 19, wherein said chromatographic medium further comprises a second enzyme detection...
- ...24. A diagnostic test kit as defined in claim 23, wherein said second detection zone is capable of capturing said25. A diagnostic test kit as defined in claim 19, wherein said chemichromic dye is a triarylmethane having the following...
- ...26. A diagnostic test kit as defined in claim 19, wherein said chemichromic dye is a diarylmethane...

3/3,KWIC/2 (Item 2 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6363424

Derwent Accession: 2006-019006

UTILITY

System for evaluating the pH and buffering capacity of moisture containing cleansing articles

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Le, Trang, Bad Soden am Taunus, DE

Sawin, Philip Andrew, Liberty Township, OH, US

Assignee: The Procter & Gamble Company, (02), Cincinnati, OH, US

Correspondence Address: THE PROCTER & GAMBLE COMPANY;INTELLECTUAL PROPERTY
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050276769	A1	20051215	US 2005153751	20050615
Provisional				US 60-579867	20040615

Fulltext Word Count: 4507

Description of the Invention:

...restore healthy, natural, substantially neutral skin conditions. The system can be used as a demonstration kit in which the consumer can perform the test by using the components provided with the system, and by following instructions provided with the system. The kit can be distributed, mailed to consumers or can be inserted into magazines or publications. The system or the corresponding demonstration kit can be useful to highlight differences between moisture containing cleansing articles (and their lotions) in...Phenol red, Neutral red, Rosolic acid, Cresol red, alpha-Naphtholphthalein, Tropeolin OOO, Thymol blue, Phenolphthalein, alpha - Naphtholbenzein, Thymolphthalein, Nile blue, Alizarin yellow, nitrazin yellow, brilliant yellow, Salicyl yellow, Diazo violet, Tropeolin O...

3/3,KWIC/3 (Item 3 from file: 654)

DIALOG(R) File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6069614 **IMAGE Available

Derwent Accession: 2005-313979

UTILITY

Method and device for detecting ammonia odors and helicobacter pylori urease infection

Inventor: Boga, RameshBabu, Roswell, GA, US

MacDonald, John Gavin, Decatur, GA, US

Assignee: Kimberly-Clark Worldwide, Inc., (02)

Correspondence Address: DORITY & MANNING, P.A., POST OFFICE BOX 1449, GREENVILLE, SC, 29602-1449, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050084977	A1	20050421	US 2003687327	20031016

Fulltext Word Count: 5747

Abstract:

...such as 4,4'-bis(dimethylamino)-benzhydrol (Michler's hydrol or BDMB), pararosaniline base and alpha - naphtholbenzein. The indicating agent is applied to a substrate which is then inserted into a tube...

Summary of the Invention:

...similar chemical structure to MH, a triamino-triphenyl-methanol dye such as pararosaniline base (PAB), alpha - naphtholbenzein or any other dye which has high sensitivity for ammonia. The dye may change color...

...Clark/Ballard Medical Devices of Draper, Utah for use in the existing H. pylori detection kits (PYtest(TM) 14C-Urea Breath Test). The use of such a balloon would help ensure...

Description of the Invention:

...Clark/Ballard Medical Devices of Draper, Utah for use in the existing H. pylori detection kits (PYtest(TM) 14C-Urea Breath Test). Such a test balloon has a volume of about...

...0062] The experiment was repeated using PAB-dye and alpha - naphtholbenzein dye instead of MH-dye. On exposure to ammonia odors, the dye-coated substrates were...

Brillux GmbH & Co. KG, (4025370), Weseler Strasse 401, 48163 Munster,
(DE), (Applicant designated States: all)

INVENTOR:

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Leusmann, Jan, Grauten Ihl 80a, 48301 Nottuln, (DE)

LEGAL REPRESENTATIVE:

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PATENT (CC, No, Kind, Date): EP 1457529 A2 040915 (Basic)
EP 1457529 A2 040915
EP 1457529 A3 041208

APPLICATION (CC, No, Date): EP 2004005200 040304;

PRIORITY (CC, No, Date): DE 10310509 030308; DE 10310511 030309; DE
10318143 030418

DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR;
HU; IE; IT; LI; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK

INTERNATIONAL PATENT CLASS (V7): C09D-005/00; C09D-007/00

TRANSLATED ABSTRACT WORD COUNT: 38

ABSTRACT WORD COUNT: 72

LANGUAGE (Publication,Procedural,Application): German; German; German

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(German)	200438	507
SPEC A	(German)	200438	1455
Total word count - document A			1962
Total word count - document B			0
Total word count - documents A + B			1962

...SPECIFICATION nach farblos bei niedrigerem pH.

Derartige Saure-Base-Indikatoren sind beispielsweise Phenolphthalein,
Nitramin, o-Kresolphthalein, (**alpha**)- **Naphtholbenzein** und
Thymolphthalein. Ein erfindungsgemas besonders geeigneter
Saure-Base-Indikator ist Phenolphthalein.

Der Saure-Base-Indikator...

...wassrige Dispersionsfarbe, in Betracht. Derartige Beschichtungsmittel
sind dem Fachmann grundsätzlich bekannt und beispielsweise in H. Kittel
"Lehrbuch der Lacke und Beschichtungen", Band 3, S. Hirzel Verlag, 2001,
Seiten 155 bis 160...

...CLAIMS der Saure-Base-Indikator ausgewählt ist aus der Gruppe bestehend
aus Phenolphthalein, Nitramin, o-Kresolphthalein, (**alpha**)-
Naphtholbenzein und Thymolphthalein.

5. Beschichtungsmittel nach einem der vorangegangenen Anspruche, dadurch
gekennzeichnet, dass der Saure-Base...

3/3,KWIC/6 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01361572

Assay for aldehyde content

Test fur Aldehyde Gehalt

Essai pour proportion d'aldehyde

PATENT ASSIGNEE:

Integrated Biomedical Technology, Inc., (2598960), 2931 Moose Trail,
Elkhart, Indiana 46514, (US), (Applicant designated States: all)

INVENTOR:

Wu, Wen H., 51819 Winding Waters Lane, Elkhart, Indiana 46514, (US)

ausgewählt aus Gummis, Agararten, Agarosen...

- ...Kieselglasern, wasserlöslichen Stärken, Polyacrylaten, Cellulosen, Cellulosederivaten, Polyethylenglycolen, Polyethylenoxiden, Polyvinylalkoholen, Dextranen, Polyacrylamiden und Polysacchariden, umfassen.
60. Kit nach Anspruch 58, wobei ein erster Gelbildner in einer oberen Lage der Immobilisierungsschicht vorgesehen ist und ein zweiter Gelbildner in einer unteren Lage der Immobilisierungsschicht vorgesehen ist.
 61. Kit nach Anspruch 41, welcher ferner Konditionierungskomponenten benachbart zu oder innerhalb der Immobilisierungsschicht zur Verbesserung der Fähigkeiten zur Mikroorganismen-Detektion umfasst.
 62. Kit nach Anspruch 61, wobei die Konditionierungskomponenten wenigstens eines von lytischen Agentien, lytischen Enzymen, grenzflächenaktiven Mitteln und Komponenten zur Neutralisation von Vermehrungsinhibitoren umfassen.
 63. Kit nach Anspruch 41, wobei die Sensorschicht Silicon umfasst.
 64. Kit nach Anspruch 41, wobei die Sensorschicht so konstruiert ist, dass sie detektierbare lokalisierte Veränderungen, die der Anwesenheit von Mikroorganismenkolonien in der Immobilisierungsschicht entsprechen, durchläuft.
 65. Kit nach Anspruch 64, wobei die Sensorschicht eine lichtundurchlässige Schicht ist, die sich in Gegenwart von Mikroorganismen von einer Farbe zu einer zweiten Farbe verändert, während sie lichtundurchlässig bleibt.
 66. Kit nach Anspruch 64, wobei wenigstens eine der Immobilisierungsschicht und der Sensorschicht lichtundurchlässig ist.
 67. Kit nach Anspruch 64, wobei wenigstens eine Schicht in der Vorrichtung Matrices aufweist, die die Visualisierung von Mikroorganismenkolonien abtraglich beeinflussen.
 68. Kit nach Anspruch 67, wobei die wenigstens eine Schicht die Sensorschicht mit umfasst.
 69. Kit nach Anspruch 64, wobei die Sensorschicht das Betrachten der Testprobe von der der Immobilisierungsschicht entgegengesetzten Seite des Sensors (der Sensorschicht) aus ausreichend blockiert.
 70. Kit nach Anspruch 64, wobei die Sensorschicht das Betrachten mit dem Auge oder das Detektieren mit...
- ...einer Blutprobe von einem Patienten und zum Detektieren von Mikroorganismen in der Blutprobe mit dem Kit von Anspruch 41, umfassend:
- a) Einführen einer Nadel in einen Patienten zum Abnehmen einer Blutprobe
- ...

3/3,KWIC/8 (Item 1 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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01324975 **Image available**

ONE-STEP ENZYMATIC AND AMINE DETECTION TECHNIQUE

DETECTION D'ENZYMES ET D'AMINES EN UNE SEULE OPERATION

Patent Applicant/Assignee:

KIMBERLY-CLARK WORLDWIDE INC, 401 N. Lake Street, Neenah, Wisconsin 54956
, US, US (Residence), US (Nationality), (For all designated states
except: US)

Patent Applicant/Inventor:

SONG Xuedong, 1135 Crabapple Lake Circle, Roswell, GA 30076, US, US

(Residence), CN (Nationality), (Designated only for: US)
BOGA RameshBabu, 1214 Hemmingway Lane, Roswell, GA 30075, US, US
(Residence), IN (Nationality), (Designated only for: US)
CHIDEBELU-EZE Chibueze Obi, 3945 Wolf Creek Circle, SW, Atlanta, GA 30331
, US, US (Residence), NG (Nationality), (Designated only for: US)

Legal Representative:

JOHNSTON Jason W et al (agent), DORITY & MANNING, P.A., P.O. Box 1449,
Greenville, SC 29602-1449, US

Patent and Priority Information (Country, Number, Date):

Patent: WO 200606960 A1 20060119 (WO 0606960)
Application: WO 2005US11050 20050331 (PCT/WO US2005011050)
Priority Application: US 2004881010 20040630

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM
ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU MC NL PL
PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 16541

Fulltext Availability:

Detailed Description
Claims

English Abstract

...amine within a test sample is provided. For example, in one
embodiment, a diagnostic test kit is employed that utilizes reactive
complexes that each includes a substrate joined (e.g., covalently...

...the reactive complexes, enzymes may cleave the substrate and release the
reporter. Moreover, the test kit may also employ a chemichromic dye,
i.e., a dye that exhibits a detectable color...

Detailed Description

... Invention

1 5 In accordance with one embodiment of the present invention, a
diagnostic test kit for detecting an amine, enzyme, or enzyme inhibitor
within a test sample (e.g., vaginal fluid) is disclosed. The kit
comprises a plurality of reactive complexes that each comprises a
substrate joined to a reporter...

...a separation species. The substrate is cleavable by an enzyme to release
the reporter. The kit further comprises a chromatographic medium that
defines a first enzyme detection zone within which an...

...of one embodiment of an assay device that may
be used in the diagnostic test kit of the present invention;
Fig. 2 is a graphical illustration of one embodiment for covalently...

...or an amine within a test sample. For example, in one embodiment, a
diagnostic test kit is employed that utilizes reactive complexes that

each includes a substrate joined (e.g., covalently...

...the reactive complexes, enzymes may cleave the substrate and release the reporter. Moreover, the test kit may also employ a chromogenic dye, i.e., a dye that exhibits a detectable color ...separation techniques, magnetic separation techniques, etc. In one particular embodiment, for example, the diagnostic test kit 0 contains an assay device that employs a chromatographic medium for separating unreacted complexes from...

...of a chromatographic medium may simplify and reduce the costs of the resulting diagnostic test kit for many consumer applications, including those in which a disposable kit is desired. Further, the use of a chromatographic medium also provides for a mechanism...

...may be simultaneously tested in a single step. That is, a user may use the kit to test a single sample for an enzyme (or inhibitor) and/or amine.

Referring to...set forth below.

OH
H₂N NH₂
H₂N

Another example of a suitable triarylmethane dye is **alpha - naphtholbenzein** and analogs thereof. **Alpha - naphtholbenzein** turns from an orange/red color to a gray/black color upon reaction with an amine. **Alpha - naphtholbenzein** contains a hydroxyl-substituted naphthyl group, a carbonyl-substituted naphthyl group, and a phenyl group. Specifically, the structure of **alpha - naphtholbenzein** is set forth below.

OH- C O
1 5
31

Still another example of a...

...pale yellow color to a blue/green color upon reaction with an amine. Similar to **alpha - naphtholbenzein**, **naphthochrome green** contains a hydroxyl-substituted naphthyl group, a carbonylsubstituted naphthyl group, and a phenyl...

...Besides diagnosing one or more types of infection in vaginal fluid, the method and diagnostic kit of the present invention may be used in any other application in which the detection...

...membrane (downstream from the first enzyme detection zone) to form a second enzyme detection zone. **Alpha - naphtholbenzein** (ANB) (5 milligrams per milliliter, Sigma-Aldrich Chemical Co., Inc.) was also striped onto the...

Claim

1. A diagnostic kit for detecting an amine, enzyme, or an enzyme inhibitor within a test sample, the kit comprising:
a plurality of reactive complexes that each comprises a substrate joined to a reporter...

...quantity of an amine is determinable from said color change. 5 2. The diagnostic test kit of claim 1, wherein said separation species is a

specific binding member.

3 The diagnostic test kit of claim 2, wherein a receptive material is immobilized within said first enzyme detection zone that has an affinity for said specific binding member.

4 The diagnostic test kit of claim 1, wherein said separation species is a magnetic particle.

5 The diagnostic test kit of claim 4, further comprising a magnetic device positioned adjacent to said chromatographic medium to immobilize said magnetic particle within a separation zone.

6 The diagnostic test kit of any of the preceding claims, wherein said substrate is a protein, glycoprotein, peptide, nucleic acid, carbohydrate, lipid, ester, or derivative thereof.

7 The diagnostic test kit of claim 6, wherein said substrate is casein, albumin, hemoglobin, myoglobin, keratin, gelatin, insulin, proteoglycan, fibronectin, laminin, collagen, elastin, or a derivative thereof.

8 The diagnostic test kit of any of the preceding claims, wherein said reporter comprises a detectable substance that is capable of directly generating said enzyme detection signal.

44

9 The diagnostic test kit of any of the preceding claims, wherein said reporter comprises a specific binding member. 10. The diagnostic test kit of claim 9, further comprising probes conjugated with a specific binding member, said probes comprising...

...or 12, wherein the test sample is obtained from vaginal fluid.

14 The diagnostic test kit or method of any of the preceding claims, wherein the enzyme is a protease or peptidase.

15 The diagnostic test kit or method of any of the preceding claims, wherein an arylmethane chernichromic dye is contained within said amine detection zone.

16 The diagnostic test kit or method of claim 15, wherein said arylmethane is a triarylmethane having the following general...

...and R" are independently selected from substituted and unsubstituted aryl groups.

17 The diagnostic test kit or method of claim 15, wherein said arylmethane

45

is a diarylmethane.

18 The diagnostic test kit or method of any of the preceding claims, wherein said amine detection zone is positioned downstream from said enzymedetection zone.

19 The diagnostic test kit or method of any of the preceding claims,

wherein the quantity of an enzyme within...

...or inversely
proportional to the intensity of said enzyme detection signal.

20 The diagnostic test kit of any of the preceding claims, wherein said chromatographic medium further comprises a second enzyme...

3/3,KWIC/9 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01320217

A SYSTEM FOR EVALUATING THE PH AND BUFFERING CAPACITY OF MOISTURE
CONTAINING CLEANSING ARTICLES

SYSTEME D'EVALUATION DU PH ET DE LA CAPACITE DE TAMPONNAGE D'ARTICLES DE
NETTOYAGE CONTENANT DE L'HUMIDITE

Patent Applicant/Assignee:

THE PROCTER & GAMBLE COMPANY, One Procter & Gamble Plaza, Cincinnati, OH
45202, US, US (Residence), US (Nationality), (For all designated states
except: US)

Patent Applicant/Inventor:

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LE Trang, Niederhofheimer Str., 19, 65812 Bad Soden, DE, DE (Residence),
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SAWIN Philip Andrew, 4975 Meadow Vista Court, Liberty Township, OH 45011,
US, US (Residence), US (Nationality), (Designated only for: US)

Legal Representative:

THE PROCTER & GAMBLE COMPANY (common-representative), c/o T. David Reed,
The Procter & Gamble Company, Winton Hill Business Center, 6110 Center
Hill Road, Cincinnati, OH 45224, US

Patent and Priority Information (Country, Number, Date):

Patent: WO 200602024 A1 20060105 (WO 0602024)

Application: WO 2005US20734 20050614 (PCT/WO US2005020734)

Priority Application: US 2004579867 20040615

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL
PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU
ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU MC NL PL
PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 4588

Fulltext Availability:

Detailed Description

Detailed Description

... restore healthy, natural, substantially neutral skin conditions. The
system can be used as a demonstration kit in which the consumer can

perform the test by using the components provided with the system, and by following instructions provided with the system. The kit can be distributed, mailed to consumers or can be inserted into magazines or publications. The system or the corresponding demonstration kit can be useful to highlight differences between moisture containing cleansing articles (and their lotions) in...

...Phenol red, Neutral red, Rosolic acid, Cresol red,
alpha-Naphtholphthalein,
Tropeolin 000, Thymol blue, Phenolphthalein, alpha - Naphtholbenzein ,
Thymolphthalein, Nile blue, Alizarin yellow, nitrazin yellow, brilliant
yellow, Salicyl yellow, Diazo violet, Tropeolin 0...

? s berthelot? (100n) nanoparticl?

886 BERTHELOT?

101463 NANOPARTICL?

S4 0 BERTHELOT? (100N) NANOPARTICL?

? b 411

14mar06 17:57:40 User228206 Session D2577.10

\$3.16 0.536 DialUnits File654

\$5.60 8 Type(s) in Format 3

\$5.60 8 Types

\$8.76 Estimated cost File654

\$1.16 0.093 DialUnits File399

\$8.25 3 Type(s) in Format 3

\$8.25 3 Types

\$9.41 Estimated cost File399

\$0.60 0.054 DialUnits File73

\$9.30 3 Type(s) in Format 3

\$9.30 3 Types

\$9.90 Estimated cost File73

\$0.20 0.044 DialUnits File144

\$0.20 Estimated cost File144

\$0.90 0.166 DialUnits File348

\$10.20 6 Type(s) in Format 3

\$10.20 6 Types

\$11.10 Estimated cost File348

\$1.13 0.239 DialUnits File349

\$8.00 5 Type(s) in Format 3

\$8.00 5 Types

\$9.13 Estimated cost File349

\$0.29 0.049 DialUnits File5

\$0.29 Estimated cost File5

\$0.12 0.034 DialUnits File94

\$1.35 1 Type(s) in Format 9

\$1.35 1 Types

\$1.47 Estimated cost File94

\$0.37 0.073 DialUnits File324

\$0.37 Estimated cost File324

OneSearch, 9 files, 1.286 DialUnits FileOS

\$0.26 TELNET

\$50.89 Estimated cost this search

\$50.89 Estimated total session cost 1.286 DialUnits

File 411:DIALINDEX(R)

DIALINDEX(R)

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*** DIALINDEX search results display in an abbreviated ***

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? sf allscience

You have 299 files in your file list.
 (To see banners, use SHOW FILES command)
 ? s ammonia? (100n) nanopartic?

Your SELECT statement is:
 s ammonia? (100n) nanopartic?

Items	File
71	2: INSPEC_1898-2006/Mar W1
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2	6: NTIS_1964-2006/Feb W4
108	8: Ei Compendex(R)_1970-2006/Mar W1
1	10: AGRICOLA_70-2006/Mar
2	14: Mechanical and Transport Engineer Abstract_1966-2006/Feb
2	15: ABI/Inform(R)_1971-2006/Mar 14
9	16: Gale Group PROMT(R)_1990-2006/Mar 14
6	20: Dialog Global Reporter_1997-2006/Mar 14
1	24: CSA Life Sciences Abstracts_1966-2006/Jan
9	31: World Surface Coatings Abs_1976-2006/Feb
167	34: SciSearch(R) Cited Ref Sci_1990-2006/Mar W1
6	35: Dissertation Abs Online_1861-2006/Feb
34	36: MetalBase_1965-20060313
1	46: Corrosion Abstracts_1966-2006/Mar
2	47: Gale Group Magazine DB(TM)_1959-2006/Mar 13
1	51: Food Sci.&Tech.Abs_1969-2006/Mar W2
6	57: Electronics & Communications Abstracts_1966-2006/Feb
2	60: ANTE: Abstracts in New Tech & Engineer_1966-2006/Feb
1	61: Civil Engineering Abstracts._1966-2006/Feb
8	62: SPIN(R)_1975-2006/Feb W4
3	65: Inside Conferences_1993-2006/Mar 14
1	67: World Textiles_1968-2006/Mar
3	68: Solid State & Superconductivity Abstracts_1966-2006/Feb
6	71: ELSEVIER BIOBASE_1994-2006/Mar W2
18	73: EMBASE_1974-2006/Mar 14
3	74: Int.Pharm.Abs_1970-2006/Feb B1
Examined 50 files	
12	94: JICST-EPlus_1985-2006/Dec W3
26	95: TEME-Technology & Management_1989-2006/Mar W2
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7	98: General Sci Abs_1984-2004/Dec
12	99: Wilson Appl. Sci & Tech Abs_1983-2006/Feb
14	103: Energy SciTec_1974-2006/Feb B2
1	104: AeroBase_1999-2006/Jan
2	136: BioEngineering Abstracts_1966-2006/Jan
95	144: Pascal_1973-2006/Feb W3
5	148: Gale Group Trade & Industry DB_1976-2006/Mar 13
1	149: TGG Health&Wellness DB(SM)_1976-2006/Feb W4
19	155: MEDLINE(R)_1951-2006/Mar 10
3	156: ToxFile_1965-2006/Feb W2
Examined 100 files	
5	211: Gale Group Newsearch(TM)_2006/Mar 13
3	240: PAPERCHEM_1967-2006/Mar W1
2	248: PIRA_1975-2006/Feb W2
1	256: TecInfoSource 82-2006/Feb
4	266: FEDRIP_2005/Dec
2	275: Gale Group Computer DB(TM)_1983-2006/Mar 13

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5    292: GEOBASE(TM)_1980-2006/Feb W4
20   293: Engineered Materials Abstracts_1966-2006/Feb
8    305: Analytical Abstracts_1980-2006/Mar W2
15   315: ChemEng & Biotec Abs_1970-2006/Feb
1    319: Chem Bus NewsBase_1984-2006/Mar 14
6    323: RAPRA Rubber & Plastics_1972-2006/Feb
1    324: German Patents Fulltext_1967-200552
2    331: Derwent WPI First View      UD=200616
Examined 150 files
48   335: Ceramic Abstracts/World Ceramics
      Abstracts_1966-2006/Feb
22   340: CLAIMS(R)/US Patent_1950-06/Mar 09
2    342: Derwent Patents Citation Indx_1978-05/200615
9    344: Chinese Patents Abs_Jan 1985-2006/Jan
2    345: Inpadoc/Fam.& Legal Stat_1968-2006/UD=200610
3    347: JAPIO Nov 1976-2005/Nov(Updated 060302)
28   348: EUROPEAN PATENTS_1978-2006/MAR
119  349: PCT FULLTEXT_1979-2006/UB=20060309,UT=20060302
3    357: Derwent Biotech Res._1982-2006/Mar W2
1    370: Science_1996-1999/Jul W3
1    390: Beilstein Facts_2005/Q3
2    391: Beilstein Reactions_2005/Q3
15   393: Beilstein Abstracts_2005/Q3
88   399: CA SEARCH(R)_1967-2006/UD=14412
207  440: Current Contents Search(R)_1990-2006/Mar 14
Examined 200 files
4    484: Periodical Abs Plustext_1986-2006/Mar W1
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2    613: PR Newswire_1999-2006/Mar 14
2    621: Gale Group New Prod.Annou.(R)_1985-2006/Mar 13
5    636: Gale Group Newsletter DB(TM)_1987-2006/Mar 13
Examined 250 files
2    647: CMP Computer Fulltext_1988-2006/Apr W1
2    649: Gale Group Newswire ASAP(TM)_2006/Mar 06
169  654: US Pat.Full._1976-2006/Mar 09
13   764: BCC Market Research_1989-2006/Feb
1    767: Frost & Sullivan Market Eng_2006/Mar

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79 files have one or more items; file list includes 299 files.

? s (ammonia? (25n) (detect? or sensor?)) and nanopartic?

Your SELECT statement is:

s (ammonia? (25n) (detect? or sensor?)) and nanopartic?

Items	File
6	2: INSPEC_1898-2006/Mar W1
1	5: Biosis Previews(R)_1969-2006/Mar W1
9	8: Ei Compendex(R)_1970-2006/Mar W1
1	9: Business & Industry(R)_Jul/1994-2006/Mar 13
1	14: Mechanical and Transport Engineer Abstract_1966-2006/Feb
2	15: ABI/Inform(R)_1971-2006/Mar 14
2	16: Gale Group PROMT(R)_1990-2006/Mar 14
3	20: Dialog Global Reporter_1997-2006/Mar 14
1	31: World Surface Coatings Abs_1976-2006/Feb
13	34: SciSearch(R) Cited Ref Sci_1990-2006/Mar W1
2	35: Dissertation Abs Online_1861-2006/Feb
3	36: MetalBase_1965-20060313
3	57: Electronics & Communications

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        Abstracts_1966-2006/Feb
1      68: Solid State & Superconductivity
        Abstracts_1966-2006/Feb
1      71: ELSEVIER BIOBASE_1994-2006/Mar W2
2      73: EMBASE_1974-2006/Mar 14
Examined 50 files
3      94: JICST-EPlus_1985-2006/Dec W3
1      95: TEME-Technology & Management_1989-2006/Mar W2
6     144: Pascal_1973-2006/Feb W3
2     148: Gale Group Trade & Industry DB_1976-2006/Mar 13
2     155: MEDLINE(R)_1951-2006/Mar 10
Examined 100 files
1     211: Gale Group Newsearch(TM)_2006/Mar 13
1     275: Gale Group Computer DB(TM)_1983-2006/Mar 13
5     305: Analytical Abstracts_1980-2006/Mar W2
1     315: ChemEng & Biotec Abs_1970-2006/Feb
Examined 150 files
3     340: CLAIMS(R)/US Patent_1950-06/Mar 09
>>>File 348 processing for SENSOR? stopped at SENSORHEIZELEMENTS
1     348: EUROPEAN PATENTS_1978-2006/MAR
>>>File 349 processing for DETECT? stopped at DETECTI4ON
>>>File 349 processing for SENSOR? stopped at SENSORHE
26    349: PCT FULLTEXT_1979-2006/UB=20060309,UT=20060302
2     357: Derwent Biotech Res._1982-2006/Mar W2
6     390: Beilstein Facts_2005/Q3
1     393: Beilstein Abstracts_2005/Q3
3     399: CA SEARCH(R)_1967-2006/UD=14412
41    440: Current Contents Search(R)_1990-2006/Mar 14
Examined 200 files
2     613: PR Newswire_1999-2006/Mar 14
2     621: Gale Group New Prod.Annou.(R)_1985-2006/Mar 13
4     636: Gale Group Newsletter DB(TM)_1987-2006/Mar 13
Examined 250 files
1     647: CMP Computer Fulltext_1988-2006/Apr W1
2     649: Gale Group Newswire ASAP(TM)_2006/Mar 06
Processing
71    654: US Pat.Full._1976-2006/Mar 09
2     763: Freedonia Market Res._1990-2006/Feb
3     764: BCC Market Research_1989-2006/Feb
1     767: Frost & Sullivan Market Eng_2006/Mar

```

42 files have one or more items; file list includes 299 files.
One or more terms were invalid in 3 files.

? save temp

Temp SearchSave "TD205028201" stored

? rf

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
---	----	----
N1	71	654: US Pat.Full._1976-2006/Mar 09
N2	41	440: Current Contents Search(R)_1990-2006/Mar 14
N3	26*	349: PCT FULLTEXT_1979-2006/UB=20060309,UT=20060302
N4	13	34: SciSearch(R) Cited Ref Sci_1990-2006/Mar W1
N5	9	8: Ei Compendex(R)_1970-2006/Mar W1
N6	6	2: INSPEC_1898-2006/Mar W1
N7	6	144: Pascal_1973-2006/Feb W3
N8	6	390: Beilstein Facts_2005/Q3
N9	5	305: Analytical Abstracts_1980-2006/Mar W2

N10 4 636: Gale Group Newsletter DB(TM)_1987-2006/Mar 13
42 files have one or more items; file list includes 299 files.
* One or more search terms are invalid in this file

- Enter P or PAGE for more -

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? p

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
N11	3	20: Dialog Global Reporter_1997-2006/Mar 14
N12	3	36: MetalBase_1965-20060313
N13	3	57: Electronics & Communications Abstracts_1966-2006/F
N14	3	94: JICST-EPlus_1985-2006/Dec W3
N15	3	340: CLAIMS(R)/US Patent_1950-06/Mar 09
N16	3	399: CA SEARCH(R)_1967-2006/UD=14412
N17	3	764: BCC Market Research_1989-2006/Feb
N18	2	15: ABI/Inform(R)_1971-2006/Mar 14
N19	2	16: Gale Group PROMT(R)_1990-2006/Mar 14
N20	2	35: Dissertation Abs Online_1861-2006/Feb

42 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

? p

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
N21	2	73: EMBASE_1974-2006/Mar 14
N22	2	148: Gale Group Trade & Industry DB_1976-2006/Mar 13
N23	2	155: MEDLINE(R)_1951-2006/Mar 10
N24	2	357: Derwent Biotech Res._1982-2006/Mar W2
N25	2	613: PR Newswire_1999-2006/Mar 14
N26	2	621: Gale Group New Prod.Annou.(R)_1985-2006/Mar 13
N27	2	649: Gale Group Newswire ASAP(TM)_2006/Mar 06
N28	2	763: Freedonia Market Res._1990-2006/Feb
N29	1	5: Biosis Previews(R)_1969-2006/Mar W1
N30	1	9: Business & Industry(R)_Jul/1994-2006/Mar 13

42 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

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Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
N31	1	14: Mechanical and Transport Engineer Abstract_1966-20
N32	1	31: World Surface Coatings Abs_1976-2006/Feb
N33	1	68: Solid State & Superconductivity Abstracts_1966-200
N34	1	71: ELSEVIER BIOBASE_1994-2006/Mar W2
N35	1	95: TEME-Technology & Management_1989-2006/Mar W2
N36	1	211: Gale Group Newsearch(TM)_2006/Mar 13
N37	1	275: Gale Group Computer DB(TM)_1983-2006/Mar 13
N38	1	315: ChemEng & Biotec Abs_1970-2006/Feb
N39	1*	348: EUROPEAN PATENTS_1978-2006/MAR
N40	1	393: Beilstein Abstracts_2005/Q3

42 files have one or more items; file list includes 299 files.

* One or more search terms are invalid in this file

- Enter P or PAGE for more -

? p

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
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N41	1	647: CMP Computer Fulltext_1988-2006/Apr W1
N42	1	767: Frost & Sullivan Market Eng_2006/Mar
N43	0	6: NTIS_1964-2006/Feb W4
N44	0	10: AGRICOLA_70-2006/Mar
N45	0	11: PsycINFO(R)_1887-2006/Mar W1
N46	0	18: Gale Group F&S Index(R)_1988-2006/Mar 13
N47	0	19: Chem.Industry Notes_1974-2006/ISS 200610
N48	0	24: CSA Life Sciences Abstracts_1966-2006/Jan
N49	0	25: Weldasearch_19662006/Feb
N50	0	28: Oceanic Abstracts_1966-2006/Jan

42 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

? p

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
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N51	0	33: Aluminium Industry Abstracts_1966-2006/Feb
N52	0	40: Enviroline(R)_1975-2005/Dec
N53	0	41: Pollution Abstracts_1966-2006/Jan
N54	0	42: Pharmaceuticl News Idx_1974-2006/Feb W3
N55	0	46: Corrosion Abstracts_1966-2006/Mar
N56	0	47: Gale Group Magazine DB(TM)_1959-2006/Mar 13
N57	0	49: PAIS Int._1976-2006/Mar
N58	0	50: CAB Abstracts_1972-2006/Feb
N59	0	51: Food Sci.&Tech.Abs_1969-2006/Mar W2
N60	0	52: TSCA Chemical Substances Inventory 2003/OCT

42 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

? p

Your last SELECT statement was:

S (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

Ref	Items	File
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N61	0	53: FOODLINE(R): Science_1972-2006/Mar 13
N62	0	54: FOODLINE(R): Market_1979-2006/Mar 13
N63	0	56: Computer and Information Systems Abstracts_1966-20
N64	0	58: GeoArchive_1974-2005/Jun
N65	0	59: FOODLINE(R): Legal_1972-2006/Mar 02
N66	0	60: ANTE: Abstracts in New Tech & Engineer_1966-2006/F
N67	0	61: Civil Engineering Abstracts._1966-2006/Feb
N68	0	62: SPIN(R)_1975-2006/Feb W4
N69	0	63: Transport Res(TRIS)_1970-2006/Feb
N70	0	64: Environmental Engineering Abstracts_1966-2006/Feb

42 files have one or more items; file list includes 299 files.

- Enter P or PAGE for more -

? b n23 n39 n29 n24 n21 n20 n19 n14 n7 n3 n1;exs

14mar06 18:02:27 User228206 Session D2577.11
\$20.38 7.690 DialUnits File411
\$20.38 Estimated cost File411
\$1.33 TELNET
\$21.71 Estimated cost this search
\$72.60 Estimated total session cost 8.977 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/Mar 10

(c) format only 2006 Dialog

*File 155: Medline has been reloaded. Some accession numbers have changed.

File 348:EUROPEAN PATENTS 1978-2006/MAR

*File 348: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.

File 5:Biosis Previews(R) 1969-2006/Mar W1

(c) 2006 BIOSIS

File 357:Derwent Biotech Res. _1982-2006/Mar W2

(c) 2006 Thomson Derwent & ISI

File 73:EMBASE 1974-2006/Mar 14

(c) 2006 Elsevier Science B.V.

File 35:Dissertation Abs Online 1861-2006/Feb

(c) 2006 ProQuest Info&Learning

File 16:Gale Group PROMT(R) 1990-2006/Mar 14

(c) 2006 The Gale Group

File 94:JICST-EPlus 1985-2006/Dec W3

(c) 2006 Japan Science and Tech Corp(JST)

File 144:Pascal 1973-2006/Feb W3

(c) 2006 INIST/CNRS

File 349:PCT FULLTEXT 1979-2006/UB=20060309,UT=20060302

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*File 349: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.

File 654:US Pat.Full. 1976-2006/Mar 09

(c) Format only 2006 Dialog

*File 654: IPCR/8 classification codes now searchable in 2006 records. For information about IC= index changes, see HELP NEWSIPCR.

Set Items Description

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Executing TD205028201

>>>SET HIGHLIGHT: use ON, OFF, or 1-5 characters

>>>File 348 processing for SENSOR? stopped at SENSORHEIZELEMENTS

>>>File 349 processing for DETECT? stopped at DETECTI4ON

>>>File 349 processing for SENSOR? stopped at SENSORHE

Processing

Processed 10 of 11 files ...

Processing

Completed processing all files

446231 AMMONIA?

6078535 DETECT?

2253842 SENSOR?

11227 AMMONIA?(25N) (DETECT? OR SENSOR?)

70473 NANOPARTIC?

S1 118 (AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?

? rd

>>>Duplicate detection is not supported for File 348.

>>>Duplicate detection is not supported for File 349.

>>>Duplicate detection is not supported for File 654.

>>>Records from unsupported files will be retained in the RD set.

S2 114 RD (unique items)

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? s s2 and kit

114 S2

417320 KIT

S3 23 S2 AND KIT

? t s3/3,kwic/all

3/3,KWIC/1 (Item 1 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01331010

COMPOSITIONS AND METHODS OF USING ANGIOPOIETIN-LIKE 4 PROTEIN

COMPOSITIONS ET METHODES D'UTILISATION DE LA PROTEINE 4 ANALOGUE A
L'ANGIOPOIETINE

Patent Applicant/Assignee:

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Patent Applicant/Inventor:

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Legal Representative:

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200614678 A2 20060209 (WO 0614678)

Application: WO 2005US25650 20050719 (PCT/WO US2005025650)

Priority Application: US 2004589875 20040720

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL
PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU
ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU LV MC NL
PL PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 41423

Fulltext Availability:

Detailed Description

Detailed Description

... markers include, procollagen type III peptide levels (PIIIP) to assess
if hepatic fibrogenesis is active; ammonia blood levels in
hepatoencephalopathies; ligand in levels in necrosis and hepatoma;

hyaluronate levels due to hepatic endothelial cell damage;
a-1-fetoprotein (APP) levels to detect hepatoma; carcinoembryonic
antigen (CEA) levels to detect cancer metastasis to the liver; elevations
of antibodies...are disclosed in Remington's Pharmaceutical Sciences,
16th edition, Oslo, A., Ed., (1980).

Liposomes and Nanoparticles

Polypeptides of the invention can be formulated in liposomes. For
example, antibodies of the invention...

...Martin et al, J. Biol. Chem. 257: 286-288 (1982) via a disulfide
interchange reaction. Nanoparticles or nanocapsules can also be used to
entrap the polypeptides of the invention. In one embodiment, a
biodegradable polyalkyl-cyanoacrylate nanoparticles can be used with the
polypeptides of the invention.

Other Uses

The anti-ANGPTL4 antibodies...of ANGPTL4, agonist or antagonist for a
disorder described herein. The instructions included with the kit
generally include information as to dosage, dosing schedule, and route of
administration for the treatment...4).

Example 4: Variant of Angptl4

A variant ANGPTL4 was made using a standard mutagenesis kit (e.g.,
QuikChange XL Site-Directed Mutagenesis Kit (Invitrogen, Carlsbad,
California)) following the manufacturer's protocol. Two amino acid
substitutions were made in...

...Isotyping Assay: The Serum Immunoglobulin Isotyping Assay was performed
using a Cytometric Bead Array (CBA) kit. This assay was used to rapidly
identify the heavy and light chains isotypes of a...

3/3,KWIC/2 (Item 2 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01210597 **Image available**

USE OF PHOSPHOPORYN FOR INDUCING BIOMINERALIZATION AND BONE REGENERATION
METHODE PERMETTANT D'INDUIRE LA BIOMINERALISATION, METHODE PERMETTANT
D'INDUIRE LA REGENERATION OSSEUSE ET METHODES ASSOCIEES

Patent Applicant/Assignee:

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, US (Nationality), (Designated only for: US)

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Legal Representative:

HEFNER Daniel M (agent), Leydig, Voit & Mayer, Ltd., Two Prudential

Plaza, Suite 4900, 180 North Stetson Avenue, Chicago, Illinois
60601-6780, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200516368 A2-A3 20050224 (WO 0516368)
Application: WO 2004US27076 20040819 (PCT/WO US04027076)
Priority Application: US 2003496245 20030819

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 24293

Fulltext Availability:

Detailed Description

Detailed Description

... under physiological conditions. All of the above variants of the
ceramic in the form of **nanoparticles** or nanocrystalline particles or
amorphous nanosized particles or gels can be chemically complexed with
the...

...to a,03 integrin (anti-cc,03) was obtained from Chemicon (Temecula, CA).
OCN ELISA kit was obtained from Zymed Laboratories (San Fransisco, CA).
PBS, ALP assay kits, alizarin red-S...

...Sigma Diagnostics, Inc. Total protein assay kits were obtained from
Bio-Rad (Hercules, CA). RNeasy Kit and DNase I were obtained from
Qiagen (Valencia, CA). RiboGreen Kit was obtained from Molecular Probes
(Eugene, OR). All quantitative real time PCR reagents, primers and...

...up-regulates osteoblast marker genes.

3 0 [001201 Total RNA was extracted using the RNeasy Kit with DNase I
treatment according to the manufacturer's protocol. RNA content was
determined using the RiboGreen RNA Quantification Kit. Conventional RNA
quantification using 260/280 absorbance readings proved to be too
imprecise to match...thawed cell lysates were incubated with 200 pL ALP
10 reagent from the Sigma Diagnostics Kit for 30 minutes at 37' C. An
initial absorbance reading (time 0) was taken at...

...analysis (EDAX).

The 21 day cultured cells were washed with de-ionized water diluted with
ammonia to prevent dissolution of any of the mineralized phases.

1 5 [001621 X-ray analysis allows the **detection** of calcium phosphate
phases which indicates the possibility of hydroxyapatite (HA) and/or
brushite formation...

DIALOG(R)File 349:PCT FULLTEXT
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01181005

**PROTEINS, SENSORS, AND METHODS OF CHARACTERIZING ANALYTES USING THE SAME
PROTEINES, CAPTEURS ET PROCEDES DE CARACTERISATION DE SUBSTANCES A ANALYSER
UTILISANT CES PROTEINES ET CES CAPTEURS**

Patent Applicant/Assignee:

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GE Xudong, 912 Hooper Avenue, Apt. D, Baltimore, MD 21229, US, US
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Legal Representative:

VAZQUEZ Rene A (et al) (agent), Fleshner & Kim, LLP, P.O. Box 221200,
Chantilly, VA 20153-1200, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 2004101769 A2-A3 20041125 (WO 04101769)

Application: WO 2004US6276 20040301 (PCT/WO US04006276)

Priority Application: US 2003469560 20030509

Designated States:

(All protection types applied unless otherwise stated - for applications
2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 25251

Fulltext Availability:

Detailed Description

Detailed Description

... may be any desirable form or shape including one or more of disk,
cylinder, patch, **nanoparticle**, microsphere, porous polymer, open cell
foam, providing it is permeable to analyte. The matrix additionally...

...and dip or spin coating) one can obtain matrices in various
configurations (e.g., granulates, **nanoparticles**, microparticles,
monoliths, and thick and thin films) suitable for *in vitro* and *in vivo*
...

...spin coating) one can obtain aerogel or xerogel-matrices in various
configurations (e.g., granulates, **nanoparticles**, microparticles,
monoliths, and thick and thin films) suitable for use *in vitro* and *in vivo*...IL). SSJ, PstI restriction enzymes were purchased from Invitrogen
Life Technologies. The Quick-Change mutagenesis kit was obtained from
Stratagene (Cedar Creek, TX).

49

Construction of the Plasmid
The plasmid...

...mutant. The single-cysteine mutation at position 255 was accomplished using the Quick-Change mutagenesis kit from Stratagene. The 5' primer used for the mutagenesis was GCACTGGCGGGCACCGTATGCAACGATGC TAAACAACC (SEQ ID NO...

...making 5-mL overnight cultures, and the plasmids were then extracted using QIAprep Spin Miniprep Kit from Qiagen. The DNA gel (not shown) confirmed the existence of the desired restriction sites...complicated process. The YSI glutamate biosensor is a glutaminase and glutamate oxidase dual enzyme sensor (www.ysi.com, which is incorporated by reference herein).

The glutamate dehydrogenase converts glutamate to glutamate and ammonia. The glutamate thus produced is then oxidized by glutamate oxidase to (alpha-ketoglutarate, ammonia, and hydrogen peroxide. The hydrogen peroxide that is released is detected at the platinum electrode. Since glutamate oxidase can also detect the glutamate that is already present in the media, the reading of the glutamine sensor...

3/3,KWIC/4 (Item 4 from file: 349)
DIALOG(R) File 349:PCT FULLTEXT
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01159817 **Image available**

METHOD OF TREATING CANCER WITH AZASPIRANE COMPOSITIONS

METHODE DE TRAITEMENT DU CANCER A L'AIDE DE COMPOSITIONS A BASE D'AZASPIRANE

Patent Applicant/Assignee:

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SHAILUBHAI Kunwar, 2707 Baldeagle Circle, Norristown, PA 19403, US, US (Residence), US (Nationality), (Designated only for: US)

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Legal Representative:

SHARER Paul L (et al) (agent), Pillsbury Winthrop LLP, P.O. Box 10500, McLean, VA 22102, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200480408 A2-A3 20040923 (WO 0480408)

Application: WO 2004US7144 20040310 (PCT/WO US04007144)

Priority Application: US 2003452951 20030310; US 2003474929 20030603

Designated States:

(All protection types applied unless otherwise stated - for applications 2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO

RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 13804

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... other ingredients known to facilitate administration and/or enhance uptake. Other formulations, such as microspheres, **nanoparticles**, liposomes, and immunologically-based systems may also be used in accordance with the present invention...healthy balance between proliferation and apoptosis in the subject's population of enterocytes.

[0070] A kit may be provide for treating cancer comprising a Compound represented by Formula I and instructions for a dosage regimen. In addition, the kit may comprising discrete quantities of the compound as well as notes/recommendations on how to...

...Cell proliferation was measured by WST- I dye conversion to Fonnazan assay using the proliferation kit from BioVision, CA. The procedure used was essentially as described in the manufacture's instructions...

...apoptotic DNA was isolated from these cells following the instructions of the DNA fragmentation analysis kit (Boehringer Mannheim Corp., Indianapolis, IN). The apoptotic DNA was evaluated using 1.5 % agarose gel...

...by resuspending cells in 200 gl (- 1 08 cells) of lysis buffer provided in the kit . Cell debris was removed by centrifugation at I 0,000 x g for 3 0...

...and was found to be 98.0% (60F254 silica gel plate; eluted in dichloromethane: methanol: **ammonia** 80:18:2; **detected** with an Isomess IM3016 radio-TLC analyzer or Phosphor Imager SF).

N

[0087] Three healthy...Cell proliferation was measured by WST-1 dye conversion to Fonnazan assay using a proliferation kit from BioVision, CA. The procedure used was essentially the same as described in the manufacture...

Claim

... R4 together with the nitrogen represent at least a 4-member heterocyclic group.

17 A kit for treating cancer comprising administering to a mammal a therapeutically effective amount of a compound...

...least a 4-member heterocyclic group; and instructions on a dosage regimen. I S. The kit of claim 17 wherein the compound is provided in discrete quantities.

19 The kit of claim 17 wherein the kit is designed for administration to humans.

20 The kit of claim 17 wherein the instruction provide notations specific to certain types of cancer.

4

3/3,KWIC/5 (Item 5 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01106090

MOLECULAR ARRAYS AND SINGLE MOLECULE DETECTION

RESEAUX MOLECULAIRES ET DETECTION DE MOLECULE UNIQUE

Patent Applicant/Assignee:

THE CHANCELLOR MASTER AND SCHOLARS OF THE UNIVERSITY OF OXFORD, The
University Offices, Wellington Square, Oxford OX1 2JD, GB, GB
(Residence), GB (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200427093 A1 20040401 (WO 0427093)

Application: WO 2003GB4041 20030919 (PCT/WO GB03004041)

Priority Application: GB 200221792 20020919; GB 200222412 20020926

Designated States:

(Protection type is "patent" unless otherwise stated - for applications
prior to 2004)

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC
SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 59626

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... particle labels. Anal Biochern. 2002 Oct 1;309(1):109-116) or by
labeling with **nanoparticles** and a number of techniques have been
developed that can start with a single molecule...or a combination of
single fluorophores.

In another embodiment the labelling scheme involves labelling with
nanoparticles. Gold **nanoparticles** which are optically active and
electronically active and can be made 1.4nm in diameter...

...dendrimer encodes a different base which is co-synthesized. The method
also provides tags comprising **nanoparticles** carrying different surface

or internal detectable groups that can be quantitatively detected.

The invention also provides tags that are composed of a string of beads, for example gold **nanoparticles**. The invention also provides tags that are composed of polymers of various lengths, the length...a single fluorescent dye molecule.

Figure 9.

Oligonucleotide target labelled with a 20nt
4 Fluosphere **nanoparticle** (Molecular Probes) hybridised to complementary molecules within a spot of a single molecule array. Individual **nanoparticles** are easily detectable distinguishable and therefore can easily be counted. Imaging was with 40X dry...

...enable interrogation using various methods. Suitable labels include: optically active dyes, such as fluorescent dyes; **nanoparticles** such as fluorospheres and quantum dots; and surface plasmon resonant particles (PRPs) or resonance light...from a single molecule assay can, for example, be amplified by labelling with dye loaded **nanoparticles**, or multi-labelled dendrimers or PRPs/SPRs. Raman spectroscopy is another means for achieving high sensitivity.

Plasmon resonant particles (PRPs) are metallic **nanoparticles** which scatter light elastically with remarkable efficiency because of a collective resonance of the conduction...

...spectrum. The magnitude, peak wavelength and spectral bandwidth of the plasmon resonance associated with a **nanoparticle** are dependent on a particle's size, shape and material composition, as well as local...

...can be used to label a molecule of interest.

SERS [Surface-enhanced Raman Scattering on **nanoparticles** exploit rarnan vibrations on metallic **nanoparticles** of the single molecules themselves to amplify their spectroscopic signatures.

Further, many of these techniques...

...use of dye molecules encounters the problems of photobleaching and blinking. Labelling with dye-loaded **nanoparticles** or surface plasmon resonance (SPR) particles reduces the problem. However a single dye molecule will...then these would be useful for encoding oligonucleotides for single molecule analysis. Fluorescently labelled latex **nanoparticles** are available from Sigma. Polystyrene beads loaded with dyes are available from molecular probes and...

...combination could be deconvoluted. Diversity could be increased by covering the QDs or dye loaded **nanoparticles** with a different characteristic that can be measured e.g. different types of functional groups...

...e.g. Kolodny et al., 2001, Anal Chem. 73: 1959-1966). Similarly PRIs or SERS **nanoparticles** can be employed in many of these ways. Recently...phosphate and a 3' Puromycin. The ligated products are in vitro translated in rabbit reticulocyte lysate kit (Ambion) for 30 minutes. The solution is adjusted to 150mM MgCl₂ and 425mM KCl to promote...individually resolvable but then the array may be functionalised so that the molecules that are detected are far enough apart to be individually resolved. This can be done as described above by destructive ammonia treatment. Alternatively, only a fraction of the molecules, each far

enough from the other to...

...provided in List A.

The probes may be linked with labels such as 20nM Fluosphere **nanoparticles** before binding to arrayed DNA or alternatively they may be biotinylated and streptavidin linked Semiconductor **Nanoparticles** can bind to them before or after the DNA is arrayed on the surface, 45 degrees C for 1 hour in Quantum Dot buffer is sufficient for this. The **nanoparticles** can be reacted with 1mg/ml BSA or casein or other appropriate blocking mix solution...

...provided by vendor Wash in PBS/Tween followed by PBS wash. Visualize DNA and fluorescent **nanoparticles** captured and horizontalised on the array.

Probing followed by horizontalisation
The target DNA can be...

...labels such as 20 DM Fluospheres.

Alternatively they may be biotinylated and streptavidin linked Semiconductor **Nanoparticles** can bind to them before or after the DNA is arrayed on the surface, 45...

...by 72 C for 10 minutes
Purify digested DNA using a commercial purification kit (Zymo Research's DNA clean and Concentrator) as per supplied protocol
Cot I DNA can...repetitive sequence.

Cot-1 DNA (Gibco BRL) is labelled with biotin using Biotin Chem-Link kit (Boehringer Mannheim) or photoprobe Biotin Kit (Vector Laboratories) as per manufacturers protocol and purified with Sephadex G50 Columns (Amersham. Pharmacia) as...

...separation is repeated, and then the target DNA supernatant is purified using a QIAex II kit (Qiagen).

In situ Blocking of Cot-1 fraction
Add 25-125ug (or 100 fold excess...

...primers using reagents for Spectral Genomics (SG) (Houston, Texas) Human BAC array and BioPrinie labelling kit from Gibco/BRL.
Add SG Sterile Water (orange vial) to xul (at least 100ng...

...using branched phosphoramidites (MWG Biotech, Germany)
There are two approaches for the use of streptavidin **nanoparticles** (Quantum Dot Corp, USA) to label probe oligonucleotides.

A Hybridise biotinylated oligonucleotide to DNA and then add streptavidin coated

nanoparticle or

B Complex streptavidin- **nanoparticle** to biotinylated oligonucleotide and hybridise to DNA In Method A there will be no steric hindrance by **nanoparticles** to hybridisation of the oligonucleotide to the target DNA. However, even though the oligonucleotide is coupled to the **nanoparticle** before hybridisation, in method B, it is not too different a situation to DNA binding to oligonucleotides bound to a surface in microarrays, which obviously works.

Preferably the **nanoparticles** need to be coupled to the oligonucleotide probes in advance of hybridisation, as in method...

...that substantially all the beads become attached with oligonucleotide (one should estimate the amount of **nanoparticle** and add oligonucleotide at e.g. 1000-10,000 excess) then unreacted oligonucleotide needs to...

...This can be done in the presence of BSA and/or other blockers. Alternatively the **nanoparticle** oligonucleotide can be reacted with lambda before combing. If this is done then, before combing...

...1000 (Clontech, USA) which can separate the long DNA target fragment from smaller products.

io **Nanoparticle** can be reacted with 1mg/ml BSA/Caesin solution to avoid absorption of the beads...

...labeled with a simple random-priming protocol based on Gibco/BRL's Bioprime DNA Labeling kit, though nick translation protocols work too. I routinely use the BioPrime labeling kit (Gibco/BRL) as a convenient and inexpensive source of random octamers, reaction buffer, and high concentration klenow (do not use the dNTP mix provided in the kit), though other sources of random primers and high concentration klenow work as well.

1. Add...

...DNA should be cleaned up by phenol/chloroform extraction / EtOH precipitation (Qiagen PCR purification kit also works well).

3o 2. Add ddH₂O or TE 8.0 to bring the total...

...50 units/ul), available through NEB or Gibco/BRL (as part of the BioPrime labeling kit), produces better labeling.

6. Incubate 37 degrees C for 1 to 2 hours, then stop...with a 100W mercury lamp can be used. Where the analysis is with AFM, then **nanoparticles** of different sizes can be used for labelling, analysis will be with tapping mode in...

...or alternatively carries a single biotin molecule or is aminated for attachment to single beads. **nanoparticles**.

In a modification, the cDNAs are labelled with incorporation of ddNTPs so that short fragments...

...are available as drop-ins for MetaMorph software. When the single molecules are labeled with **nanoparticles** the camera and objectives may be of a lower grade.

Total Internal Reflection Microscopy (TIRF...silver ions are reduced by hydroquinone to silver metal at the surfaces of the gold **nanoparticles**.

Adding gold particles with a positively charged surface coating such as lysine which bind by...

Claim

... according to claim 15 or claim 16 wherein the label is a non-fluorescent molecule, **nanoparticle** or nanorod.

19 A method according to any one of claims 1 to 18 wherein...

...chemistry. 128. A method according to claim 126 wherein the tag is selected from a nanoparticle, a nanorod and a quantum dot. 129. A method according to any one of claims...

3/3,KWIC/6 (Item 6 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01087035 **Image available**

USE OF UREASE FOR INHIBITING CANCER CELL GROWTH

UTILISATION D'UREASE POUR INHIBER LA CROISSANCE DE CELLULES CANCEREUSES

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200409112 A1 20040129 (WO 0409112)

Application: WO 2003CA1061 20030716 (PCT/WO CA03001061)

Priority Application: US 2002397244 20020718

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ
EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD
SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 28718

Fulltext Availability:

Detailed Description

Detailed Description

... or to assess changes in tumor size or extent during treatment.

Also disclosed is a kit for use in inhibiting growth of cancer cells in a io mammalian subject. The kit has a pharmaceutical composition containing urease enzyme, and instructional materials teaching the administration of the... 1 @Lm) may be designed using polymers able to be degraded in vivo. Biodegradable polyisobutylcyanoacrylate nanoparticles that meet these requirements are contemplated for use in the present invention, and such particles...

...al.

(2001) Int J Pharm 214(1-2):13 Methods of preparing polyalkyl-cyano-acrylate nanoparticles containing biologically active substances and their use are

34

described in U.S. Pat. Nos...and diagnosis of various cancer types. Kits, as described below, are also contemplated, wherein the kit comprises a dosage form of a

59

pharmaceutical composition and a package insert containing instructions ...

...effective to reach the tumor site. The urease hydrolyzes the labelled urea to produce labelled ammonia, which could be detected on the scan.

VI. Kits

In still another aspect, this invention provides kits for inhibiting...

...the use of active agents for inhibiting tumor cell growth.

Thus, in one embodiment, the kit includes a pharmaceutical composition containing an active agent, preferably a urease enzyme, and instructional materials...

3/3,KWIC/7 (Item 7 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01009846 **Image available**

AN ENZYME-BASED SYSTEM AND SENSOR FOR MEASURING ACETONE

SYSTEME A BASE D'ENZYMES ET CAPTEUR SERVANT A DETECTER L'ACETONE

Patent Applicant/Assignee:

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200339483 A2-A3 20030515 (WO 0339483)
Application: WO 2002US36028 20021108 (PCT/WO US02036028)
Priority Application: US 2001332349 20011109

Designated States:

(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM DZ EC
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT
LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL
TJ TM TN TR TT TZ UA UG US UZ YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 38857

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... assess oxidative stress or early cancer detection.

In a preferred embodiment of the invention, a kit for detecting acetone in a sample includes an acetone-specific enzyme system and a housing single disposable unit within the kit .

The present invention also provides a secondary alcohol dehydrogenase enzyme that is a protein obtained...as used herein, indicates platinum-coated carbon, for example at least partially platinum-coated carbon nanoparticles .

"Photometric," as used herein, indicates any detection mode in which photons are ...among the most commonly used in clinical chemistry (Carr and Bowers, 1980). A commercially available kit uses the dye Amplex Red for fluorescence detection of H₂O₂ (Haugland, 2002).

Any fluorescent dyes...yield for this reaction is very high; 10-14 mol ATP can be detected. A kit for this reaction is commercially available (Haugland, 2002). Because luciferase is the enzyme that causes...by TD Rhines and MA Arnold, Fiber-optic biosensor for urea based on sensing of ammonia gas, Anal Chim. Acta, 1989, 227:387; several enzyme-based amperometric NH₄⁺ sensors are commercially available. For acetone

40

detection , ammonia production can be coupled to the secondary alcohol dehydrogenase system as above; ammonia concentration would then be proportional to acetone concentration. Another enzyme scheme to couple acetone to...of Toray carbon paper (porous carbon paper) or cloth, loaded with 20% (w/w) platinum nanoparticles (these platinum nanoparticleloaded paper or cloth was purchased from ETEK Division of De Nora North America, i 0...carbon cloth or paper to which was bound highly conductive graphite particle loaded with platinum nanoparticles (10 to 20% (w/w) loading). The cloth or paper was hole-punched ...correlating acetone production with blood bioavailability of a drug of interest.

Also contemplated is a kit for detecting acetone in a sample comprising the acetone-specific enzyme system separate from, or...

Claim

... 3 1, wherein the medical condition being monitored is diabetes or weight loss.

33 A kit for detecting acetone in a sample, the kit comprising at least one acetone-specific enzyme system which includes an enzyme that selectively targets acetone...

...mediator; and a housing for the at least one acetone-specific enzyme system.

34 The kit according to claim 33 further containing a disposable test strip upon which the acetone-specific enzyme system is disposed.

123

. The kit according to claim 34, wherein the strip is separate from the housing such that the be introduced.

36 The kit according to claim 34, wherein the strip and the housing for the strip are fashioned...

3/3,KWIC/8 (Item 8 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01009773 **Image available**

HAND-HELD MEDICAL APPARATUS

APPAREIL MEDICAL PORTATIF

Patent Applicant/Assignee:

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Patent Applicant/Inventor:

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CRANLEY Paul E, 56 Yaupon Court, Lake Jackson, TX 77566, US, US (Residence), US (Nationality), (Designated only for: US)

DANOWSKI Kristine L, 122 Vail Street, Midland, MI 48642, US, US (Residence), US (Nationality), (Designated only for: US)

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SHICK Reed A, 2470 E. Newcastle Lane, Midland, MI 48640, US, US (Residence), US (Nationality), (Designated only for: US)

SUN Larry, 71 Royal Crescent, Sarnia, Ontario N7S 4Z4, CA, CA (Residence), CA (Nationality), (Designated only for: US)

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200339367 A1 20030515 (WO 0339367)

Application: WO 2002US36027 20021108 (PCT/WO US0236027)

Priority Application: US 2001332349 20011109

Designated States:

(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM DZ EC
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT
LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL
TJ TM TN TR TT TZ UA UG US UZ YU ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 20887

Fulltext Availability:

Detailed Description

Detailed Description

... as used herein, indicates platinum-coated carbon, for example at least partially platinum-coated carbon **nanoparticles** .

"Photometric," as used herein, indicates any detection mode in which photons are utilized and includes...among the most commonly used in clinical chemistry (Carr and Bowers, 1980). A commercially available kit uses the dye Amplex Red for fluorescence detection of H₂O₂ (Haugland, 2002).

Any fluorescent dyes...yield for this reaction is very high; 10-14 mol ATP can be detected. A kit for this reaction is commercially available (Haugland, 2002). Because luciferase is the enzyme that causes...by TD Rhines and MA Arnold, Fiber-optic biosensor for urea based on sensing of **ammonia** gas, Anal Chim. Acta, 198% 227:387; several enzyme-based amperometric NH₄⁺ sensors are commercially available. For acetone detection , **ammonia** production can be coupled to the secondary alcohol dehydrogenase system as above; **ammonia** concentration would then be proportional to acetone concentration. Another enzyme scheme to couple acetone to...of Toray carbon paper (porous carbon paper) or cloth, loaded with 20% (w/w) platinum **nanoparticles** (these platinum particles are nanonoparticles deposited on carbon; the platinum **nanoparticle**loaded paper or cloth was purchased from ETEK Division of De Nora North America, Somerset, NJ...

3/3,KWIC/9 (Item 1 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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6438209 **IMAGE Available

UTILITY

Novel human hydrolase family members and uses thereof

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Assignee: Millennium Pharmaceuticals Inc., (02)

Correspondence Address: MILLENNIUM PHARMACEUTICALS, INC., 40 Landsdowne Street, CAMBRIDGE, MA, 02139, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060035362	A1	20060216	US 2005244219	20051005
Division	ABANDONED			US 2002193452	20020711
CIP	ABANDONED			US 2001816664	20010323
Provisional				US 60-191973	20000324
Provisional				US 60-199559	20000425
Provisional				US 60-206036	20000522
Provisional				US 60-205442	20000519
Provisional				US 60-209949	20000606

Provisional	US 60-214948	20000629
Provisional	US 60-220008	20000721
Provisional	US 60-220040	20000721
Provisional	US 60-226774	20000821
Provisional	US 60-235033	20000925
Provisional	US 60-238170	20001005
Provisional	US 60-267054	20010207
Provisional	US 60-213688	20000623

Fulltext Word Count: 42296

Description of the Invention:

...effect of the expression of the mutant on the 26443 or 46873 substrate can be **detected**, e.g., by measuring fatty the amount of asparagine and/or aspartic acid and **ammonia**. Plasmid DNA can then be recovered from the cells that score for inhibition, or alternatively... wild type protein (e.g., altered cellular levels of asparagine and/or aspartic acid and **ammonia**). Moreover, the anti-26443 or -46873 antibodies of the invention can be used to **detect** and isolate 26443 or 46873 proteins, regulate the bioavailability of 26443 or 46873 proteins, and...from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates...for detecting the presence of 26443 or 46873 in a biological sample. For example, the kit can include a compound or agent capable of detecting 26443 or 46873 protein or mRNA...

...and a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect 26443 or 46873 protein or nucleic acid...

...0261] For antibody-based kits, the kit can include: (1) a first antibody (e.g., attached to a solid support) which binds...

...0262] For oligonucleotide-based kits, the kit can include: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a...useful for amplifying a nucleic acid molecule corresponding to a marker of the invention. The kit can also includes a buffering agent, a preservative, or a protein-stabilizing agent. The kit can also includes components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples that can be assayed and compared to the test sample contained. Each component of the kit can be enclosed within an individual container and all of the various containers can be...

...single package, along with instructions for interpreting the results of the assays performed using the kit.

[...solid support, e.g., to different addresses of an array or to different beads or **nanoparticles**.

[

Non-exemplary or Dependent Claim(s):

...11. A kit comprising a compound which selectively binds to a polypeptide of claim 5 and instructions for...14. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and...

3/3,KWIC/10 (Item 2 from file: 654)
DIALOG(R)File 654:US Pat.Full.
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6432841
Derwent Accession: 2002-075167
UTILITY

Methods of obtaining epothilone D using crystallization and /or by the culture of cells in the presence of methyl oleate
Inventor: Arslanian, Robert L., Pacifica, CA, US
Assignee: Kosan Biosciences, Inc., (02), Hayward, CA, US
Examiner: Kerr, Kathleen
Legal Representative: Townsend and Townsend and Crew LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6998256	B2	20060214	US 2001957483	20010919
Related Publ	US 20030073205	A1	20030417		
CIP	PENDING			WO 2001US13793	20010426
CIP	PENDING			US 2001825856	20010403
CIP	PENDING			US 2001825857	20010403
CIP	PENDING			US 2000560367	20000428
Provisional				US 60-269020	20010213
Provisional				US 60-257517	20001221
Provisional				US 60-232696	20000914

US Term Extension: 387 days

Fulltext Word Count: 55808

Summary of the Invention:

...0299] Where applicable, the inventive compounds may be formulated as microcapsules and nanoparticles . General protocols are described for example, by Microcapsules and Nanoparticles in Medicine and Pharmacy by Max Donbrow, ed., CRC Press (1992) and by U.S...cells are embedded in agarose and lysed according to the BIO-RAD genomic DNA plug kit . DNA plugs are partially digested with restriction enzyme, such as Sau3AI or HindIII, and electrophoresed...for 5 min. The supernatant was then used for ammonia analysis with an ammonia assay kit (Sigma). Samples were diluted 20-100 fold with water until the final concentrations were less ...With the consumption of casitone by the cells, a gradual accumulation of ammonium was also detected in the production medium. The final ammonia concentration approached 20 mM at the end of the 5-day fermentation...

3/3,KWIC/11 (Item 3 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6323780 **IMAGE Available
Derwent Accession: 2004-690468
UTILITY

Method of treating cancer with azaspirane compositions
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Jacob, Gary S., New York, NY, US
Picker, Donald H., Forrest Hills, NY, US

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050250801	A1	20051110	US 2004796292	20040310
Provisional				US 60-452951	20030310
Provisional				US 60-474929	20030603

Fulltext Word Count: 11567

Description of the Invention:

...other ingredients known to facilitate administration and/or enhance uptake. Other formulations, such as microspheres, **nanoparticles**, liposomes, and immunologically-based systems may also be used in accordance with the present invention0082] A kit may be provide for treating cancer comprising a Compound represented by Formula I and instructions for a dosage regimen. In addition, the kit may comprising discrete quantities of the compound as well as notes/recommendations on how to...Cell proliferation was measured by WST-1 dye conversion to Formazan assay using the proliferation kit from BioVision, CA. The procedure used was essentially as described in the manufacture's instructions...apoptotic DNA was isolated from these cells following the instructions of the DNA fragmentation analysis kit (Boehringer Mannheim Corp., Indianapolis, Ind.). The apoptotic DNA was evaluated using 1.5% agarose gel...200 [small mu, Greek]l (~10⁸ cells) of lysis buffer provided in the kit. Cell debris was removed by centrifugation at 10,000Xg for 30 min. Supernatants (50-100...and was found to be 98.0% (60F254 silica gel plate; eluted in dichloromethane: methanol: ammonia 80:18:2; detected with an Isomess IM-3016 radio-TLC analyzer or Phosphor Imager SF...Cell proliferation was measured by WST-1 dye conversion to Formazan assay using a proliferation kit from BioVision, CA. The procedure used was essentially the same as described in the manufacture...

Exemplary or Independent Claim(s):

...17. A kit for treating cancer comprising administering to a mammal a therapeutically effective amount of a compound...

Non-exemplary or Dependent Claim(s):

...18. The kit of claim 17 wherein the compound is provided in ...19.
The kit of claim 17 wherein the kit is designed for administration to humans...

...20. The kit of claim 17 wherein the instruction provide notations specific to certain types of cancer.

3/3,KWIC/12 (Item 4 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6315547

Derwent Accession: 2004-295431

UTILITY

Molecular arrays and single molecule detection

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Assignee: The Chancellor, Master and Scholars of The University of Oxford,
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050244863	A1	20051103	US 200585679	20050321
Continuation	UNKNOWN			WO 2003GB4041	20030919
Priority				GB 200221792	20020919
				GB 200222412	20020926

Fulltext Word Count: 60084

Summary of the Invention:

...particle labels. Anal Biochem. 2002 Oct. 1;309(1):109-116) or by labeling with **nanoparticles** and a number of techniques have been developed that can start with a single molecule...0189] In another embodiment the labelling scheme involves labelling with **nanoparticles**. Gold **nanoparticles** which ...dendrimer encodes a different base which is co-synthesized. The method also provides tags comprising **nanoparticles** carrying different surface or internal detectable groups that can be quantitatively detected...

...invention also provides tags that are composed of a string of beads, for example gold **nanoparticles**. The invention also provides tags that are composed of polymers of various lengths, the length...

Description of the Invention:

0231] Oligonucleotide target labelled with a 20 nM Fluosphere **nanoparticle** (Molecular Probes) hybridised to complementary molecules within a spot of a single molecule array. Individual **nanoparticles** are easily detectable distinguishable and therefore can easily be counted. Imaging was with 40X dry...enable interrogation using various methods. Suitable labels include: optically active dyes, such as fluorescent dyes; **nanoparticles** such as fluorospheres and quantum dots; and surface plasmon resonant particles (PRPs) or resonance light...from a single molecule assay can, for example, be amplified by labelling with dye loaded **nanoparticles**, or multi-labelled dendrimers or PRPs/SPRs. Raman spectroscopy is another means for achieving high...

...0300] Plasmon resonant particles (PRPs) are metallic **nanoparticles** which scatter light elastically with remarkable efficiency because of a collective resonance of the conduction...

...spectrum. The magnitude, peak wavelength and spectral bandwidth of the plasmon resonance associated with a **nanoparticle** are dependent on a particle's size, shape and material composition, as well as local0301] SERS [Surface-enhanced Raman Scattering on **nanoparticles** exploit raman vibrations on metallic **nanoparticles** of the single molecules themselves to amplify their spectroscopic signatures...

...use of dye molecules encounters the problems of photobleaching and blinking. Labelling with dye-loaded **nanoparticles** or surface plasmon resonance (SPR) particles reduces the problem. However a single dye molecule will...then these would be useful for encoding oligonucleotides for single molecule analysis. Fluorescently labelled latex **nanoparticles** are available from Sigma. Polystyrene beads loaded with dyes are

available from molecular probes and...combination could be deconvoluted. Diversity could be increased by covering the QDs or dye loaded **nanoparticles** with a different characteristic that can be measured e.g. different types of functional groups...

...e.g. Kolodny et al., 2001, Anal Chem. 73: 1959-1966). Similarly PRPs or SERS **nanoparticles** can be employed in many of these ways. Recently quantum nanobars have been reported. These...phosphate and a 3' Puromycin. The ligated products are in vitro translated in rabbit reticulocyte lysate kit (Ambion) for 30 minutes. The solution is adjusted to 150 mM MagCl₂ and...individually resolvable but then the array may be functionalised so that the molecules that are **detected** are far enough apart to be individually resolved. This can be done as described above by destructive ammonia treatment. Alternatively, only a fraction of the molecules, each far enough from the other to...0666] The probes may be linked with labels such as 20 nm Fluosphere **nanoparticles** before binding to arrayed DNA or alternatively they may be biotinylated and streptavidin linked Semiconductor **Nanoparticles** can bind ...45 degrees C for 1 hour in Quantum Dot buffer is sufficient for this. The **nanoparticles** can be reacted with 1 mg/ml BSA or caesin or other appropriate blocking mix...

...provided by vendor Wash in PBS/Tween followed by PBS wash. Visualize DNA and fluorescent **nanoparticles** captured and horizontalised on the array ...labels such as 20 nm Fluospheres. Alternatively they may be biotinylated and streptavidin linked Semiconductor **Nanoparticles** can bind to them before or after the DNA is arrayed on the surface, 450689] Purify digested DNA using a commercial purification kit (Zymo Research's DNA clean and Concentrator) as per supplied protocol...

...0692] Cot-1 DNA (Gibco BRL) is labelled with biotin using Biotin Chem-Link kit (Boehringer Mannheim) or photoprobe Biotin Kit (Vector Laboratories) as per manufacturers protocol and purified with Sephadex G50 Columns (Amersham Pharmacia) as...separation is repeated, and then the target DNA supernatant is purified using a QIAex II kit (Qiagen...primers using reagents for Spectral Genomics (SG) (Houston, Texas) Human BAC array and BioPrime labelling kit from Gibco/BRL...0000] **Nanoparticle** Bioconjugation and Purification...0710] There are two approaches for the use of streptavidin **nanoparticles** (Quantum Dot Corp, USA) to label probe oligonucleotides...

...0711] A Hybridise biotinylated oligonucleotide to DNA and then add streptavidin coated **nanoparticle** or 0712] B Complex streptavidin-**nanoparticle** to biotinylated oligonucleotide and hybridise to DNA...

...0713] In Method A there will be no steric hindrance by **nanoparticles** to hybridisation of the oligonucleotide to the target DNA. However, even though the oligonucleotide is coupled to the **nanoparticle** before hybridisation, in method B, it is not too different a situation to DNA binding to oligonucleotides bound to a surface in microarrays, which obviously works. Preferably the **nanoparticles** need to be coupled to the oligonucleotide probes in advance of hybridisation, as in method...

...that substantially all the beads become attached with oligonucleotide (one should estimate the amount of **nanoparticle** and add oligonucleotide at e.g. 1000-10,000 excess) then unreacted oligonucleotide needs to 0719] A **nanoparticle** attached oligonucleotide probe can be reacted with sample (e.g. lambda) DNA that has already...

...This can be done in the presence of BSA and/or other blockers.

Alternatively the **nanoparticle** oligonucleotide can be reacted with lambda before combing. If this is done then, before combing...

...0720] **Nanoparticle** can be reacted with 1 mg/ml BSA/Caeson solution to avoid absorption of the...labeled with a simple random-priming protocol based on Gibco/BRL's Bioprime DNA Labeling kit , though nick translation protocols work too. I routinely use the BioPrime labeling kit (Gibco/BRL) as a convenient and inexpensive source of random octamers, reaction buffer, and high concentration klenow (do not use the dNTP mix provided in the kit), though other sources of random primers and high concentration klenow work as well...

...the DNA should be cleaned up by phenol/chloroform extraction/EtOH precipitation (Qiagen PCR purification kit also works well...

Non-exemplary or Dependent Claim(s):

...18. A method according to claim 15 wherein the label is a non-fluorescent molecule, **nanoparticle** or nanorod...94. A method according to claim 92 wherein the tag is selected from a **nanoparticle** , a nanorod and a quantum dot...

3/3,KWIC/13 (Item 5 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6069614 **IMAGE Available
Derwent Accession: 2005-313979
UTILITY

Method and device for detecting ammonia odors and helicobacter pylori urease infection

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	Publication Number	Kind	Date	Application Number	Filing Date
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Main Patent	US 20050084977	A1	20050421	US 2003687327	20031016

Fulltext Word Count: 5747

Method and device for detecting ammonia odors and helicobacter pylori urease infection

Abstract:

...patient blows into the tube or straw, the indicating agent will change color if it **detects** levels of **ammonia** which are consistent with helicobacter pylori urease infection.

Summary of the Invention:

...0001] The present invention relates to a method and device for **detecting ammonia** odors and uses thereof, in particular for diagnosing helicobacter pylori urease infection...

...to be the cause of most stomach ulcers and ulcers of the duodenum and,

once detected , can be cured by treatment with antibiotics. H. pylori (HP) produces an active form of the urease enzyme, which hydrolyzes urea into ammonia and carbon dioxide. Since ammonia is the key component generated by urease-catalyzed hydrolysis of...

...0003] However, there are not many systems to detect ammonia odors, and of those available, most require the use of expensive instrumentation and are complex...

...need for a simple, safe device which needs neither expensive instrument nor radioactive materials for detecting ammonia from HPU infection and other sources...

...0007] This invention describes a simple device for detecting ammonia odors using a visual indicating agent which changes color when ammonia is present in the breath of a user, in particular when the ammonia is present in the range of 20 to 500 parts per million (ppm), more preferably...

...ingest urea prior to his or her breath being tested so as to boost the ammonia levels which are detected . After a period of time sufficient to allow HPU, if present, to hydrolyze the urea into ammonia and carbon dioxide, the patient would then blow into a breath testing device. If the patient were infected with HPU, sufficient amounts of ammonia would be present in his or her breath to be detected by the device, and the indicating agent would show a change in color.

Description of the Invention:

...0018] FIG. 1 shows a standard curve for the detection of ammonia by Michler's Hydrol-dye...

...0019] FIG. 2 shows a standard curve for the detection of ammonia by pararosaniline base (PAB...

...0026] The invention provides simple breath testing devices which are able to detect levels of ammonia odors in a patient's breath which are consistent with helicobacter pylori urease infection without...

...0032] The substrate, typically a cellulose tissue, may also be coated with nanoparticles to provide a high surface area coating on the substrate, i.e., higher than the...

...the cellulose tissue may be given a boost in surface area by coating it with nanoparticles . The treated substrate may be then coated with the visual indicating dye. It's believed...

...0033] The average size of the nanoparticles is generally less than about 100 nanometers, in fact it may be from about 1...

...0034] The nanoparticles may have a surface area of from about 50 square meters per gram (m²/g)...

...0035] In addition, the nanoparticles may also be relatively nonporous or solid. That is, the nanoparticles may have a pore volume that is less than about 0.5 milliliters per gram...

...mug. It is believed that the solid nature, i.e., low pore volume, of the nanoparticles may enhance the uniformity and stability of the nanoparticles .

[...

- ...0036] Examples of commercially available alumina **nanoparticles** include, for instance, Aluminasol(R) 100, Aluminasol(R) 200 and Aluminasol(R) 520, which are available from Nissan Chemical America Corporation of Houston, Tex., USA. Alternatively, silica **nanoparticles** may be utilized, such as Snowtex-C(R), Snowtex-O(R), Snowtex-PS(R) and Snowtex-OXS(R) **nanoparticles**, which are also available from Nissan Chemical...
- ...0037] Snowtex-OXS(R) **nanoparticles**, for instance, have a particle size of from 4 to 6 nanometers, and may be...
- ...per gram. Also, alumina-coated silica particles may be used, such as Snowtex-AK(R) **nanoparticles** available from Nissan Chemical...
- ...ingest urea prior to his or her breath being tested so as to boost the **ammonia** levels which are **detected**. After a period of time sufficient to allow HPU, if present, to hydrolyze the urea into **ammonia** and carbon dioxide, the patient would then blow into the breath testing device. If the patient were infected with HPU, sufficient amounts of **ammonia** would be present in his or her breath to be **detected** by the device, and the indicating agent would show a change in color...
- ...R) tissues from Kimberly-Clark Corporation of Neenah, Wis., were coated with Snowtex-O(R) **nanoparticles** (pH 4.1), available from Nissan Chemical and were used in the examples described herein...
- ...axis is the absorbance at 590 nm from 1 to 0.7. The sensitivity of **ammonia** **detection** by MH was shown to be very high...
- ...0060] A first embodiment of a device 10 for **detecting** HPU infection was designed using an **ammonia** -odor sensitive dye coated on a cellulose substrate (FIG. 4). Accordingly, 1 mg/ml stock...
- ...had been previously coated with a 1 weight percent (dry) solution of SNOWTEX-O(R) **nanoparticles** and allowed to air dry. The dye-coated paper towel was then cut into 2...
- ...of the indicating dye showed a clear difference between before and after the exposure to **ammonia** odors (~100 ppb). The level of **detection** of **ammonia** odor by either MH or PAB (~100 ppb) is far less compared to the physiological...
- ...0067] KIMWIPES(R) tissues were coated with a 5% Snowtex-O(R) **nanoparticle** solution from Nissan Chemical and then air-dried. 5.0 mg/ml stock solution of MH-dye in acetonitrile was applied to the Snowtex-O **nanoparticle** -coated KIMWIPES(R) tissues and a blue color was observed to develop as the applied...
- ...Oakland, Calif., was placed on a cardboard strip 22, and a piece of the dye- **nanoparticle** coated tissue 24 was placed over a first end 25 of the straw. Thus, when...
- ...0073] In order to ensure that the HPU testing devices as described above would **detect** the levels of **ammonia** which are exhaled by patients having ulcers, it is preferable that a uniform amount of...
- ...0074] From the above examples, it can be seen that it is possible to **detect** HPU infection using a visual indicating agent which is sensitive to **ammonia** and/or amine odors, rather than requiring a patient to ingest radioactive materials and to

Exemplary or Independent Claim(s):

1. A breath testing device for detecting the presence of ammonia odors, comprising a visual indicating agent that is color sensitive to ammonia .

...

- ...24. A kit for detecting helicobacter pylori urease infection which comprises a breath testing device having a visual indicating agent that is color sensitive to ammonia and a breath collecting device

Non-exemplary or Dependent Claim(s):

- ...12. The breath testing device of claim 10, further comprising nanoparticles .

3/3,KWIC/14 (Item 6 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6069558

Derwent Accession: 2003-532602

UTILITY

Enzyme-based system and sensor for measuring acetone

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Assignee: Unassigned

Correspondence Address: THE DOW CHEMICAL COMPANY;INTELLECTUAL PROPERTY
SECTION, P. O. BOX 1967, MIDLAND, MI, 48641-1967, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050084921	A1	20050421	US 2004494923	20040505
PCT	WO PCT/US02/36	00000000			
Provisional				US 60-332349	20011109

Fulltext Word Count: 39145

Summary of the Invention:

...0062] In a preferred embodiment of the invention, a kit for detecting acetone in a sample includes an acetone-specific enzyme system and a housing...

...system may be fashioned into the housing to form a single disposable unit within the kit .

[

Description of the Invention:

...as used herein, indicates platinum-coated carbon, for example at

least partially platinum-coated carbon nanoparticles .

[...among the most commonly used in clinical chemistry (Carr and Bowers, 1980). A commercially available kit uses the dye Amplex Red for fluorescence detection of H_2O_2 (Haugland...

...for this reaction is very high; 10^{-14} mol ATP can be detected. A kit for this reaction is commercially available (Haugland, 2002). Because luciferase is the enzyme that causes...

...D Rhines and M A Arnold, Fiber-optic biosensor for urea based on sensing of ammonia gas, Anal Chim. Acta, 1989, 227:387; several enzyme-based amperometric NH_4^+ sensors are commercially available. For acetone detection , ammonia production can be coupled to the secondary alcohol dehydrogenase system as above; ammonia concentration would then be proportional to acetone concentration. Another enzyme scheme to couple acetone to...of Toray carbon paper (porous carbon paper) or cloth, loaded with 20% (w/w) platinum nanoparticles (these platinum particles are nanonparticles deposited on carbon; the platinum nanoparticle -loaded paper or cloth was purchased from ETEK Division of De Nora North America, Somerset...carbon cloth or paper to which was bound highly conductive graphite particle loaded with platinum nanoparticles (10 to 20% (w/w) loading). The cloth or paper was hole-punched and attached...0262] Also contemplated is a kit for detecting acetone in a sample comprising the acetone-specific enzyme system separate from, or...

Exemplary or Independent Claim(s):

...33. A kit for detecting acetone in a sample, the kit comprising at least one acetone-specific enzyme system which includes an enzyme that selectively targets...

Non-exemplary or Dependent Claim(s):

...34. The kit according to claim 33 further containing a disposable test strip upon which the acetone-specific...

...35. The kit according to claim 34, wherein the strip is separate from the housing such that the...

...36. The kit according to claim 34, wherein the strip and the housing for the strip are fashioned...

3/3,KWIC/15 (Item 7 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

0005887254 **IMAGE Available

Derwent Accession: 2003-441447

Hand-held medical apparatus

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McIntyre, James, INV

Schick, Reed, INV

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Publication

Application

Filing

	Number	Kind	Date	Number	Date
Main Patent	US 20040236244	A1	20041125	US 2004492953	20040415
PCT					
Provisional				US 60-332349	20011109

Fulltext Word Count: 22272

Description of the Invention:

...as used herein, indicates platinum-coated carbon, for example at least partially platinum-coated carbon **nanoparticles** .

[...among the most commonly used in clinical chemistry (Carr and Bowers, 1980). A commercially available kit uses the dye Amplex Red for fluorescence detection of H₂O₂ (Haugland...

...for this reaction is very high; 10¹⁴ mol ATP can be detected. A kit for this reaction is commercially available (Haugland, 2002). Because luciferase is the enzyme that causes...

...TD Rhines and M A Arnold, Fiber-optic biosensor for urea based on sensing of **ammonia** gas, Anal Chim. Acta, 1989, 227:387; several enzyme-based amperometric NH₄⁺ **sensors** are commercially available. For acetone **detection** , **ammonia** production can be coupled to the secondary alcohol dehydrogenase system as above; **ammonia** concentration would then be proportional to acetone concentration. Another enzyme scheme to couple acetone to...of Toray carbon paper (porous carbon paper) or cloth, loaded with 20% (w/w) platinum **nanoparticles** (these platinum particles are nanonoparticles deposited on carbon; the platinum **nanoparticle** -loaded paper or cloth was purchased from ETEK Division of De Nora North America, Somerset...

3/3,KWIC/16 (Item 8 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

0005851516 **IMAGE Available

Derwent Accession: 2004-765633

Novel human hydrolase family members and uses thereof

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Rudolph-Owen, Laura, INV

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040214758	A1	20041028	US 2002193452	20020711
CIP	ABANDONED			US 2001816664	20010323
Provisional				US 60-191973	20000324
Provisional				US 60-199559	20000425
Provisional				US 60-206036	20000522
Provisional				US 60-205442	20000519
Provisional				US 60-209949	20000606
Provisional				US 60-214948	20000629
Provisional				US 60-220008	20000721
Provisional				US 60-220040	20000721

Provisional	US 60-226774	20000821
Provisional	US 60-235033	20000925
Provisional	US 60-238170	20001005
Provisional	US 60-267054	20010207
Provisional	US 60-213688	20000623

Fulltext Word Count: 605801

Description of the Invention:

...more of the following activities: (1) catalyzes the hydrolysis of asparagine to aspartic acid and ammonia ; (2) regulates cellular amounts of asparagine; (3) regulates the cellular amounts of aspartic acid; (4) regulates cellular amounts of ammonia ; and (5) antagonizes or inhibits, e.g., competitively or noncompetitively, any of activities 1-4...

...asparaginase family members. Asparaginase enzymes assist in the hydrolysis of asparagine to aspartic acid and ammonia . Thus, the 26443 or 46873 molecules can act as novel diagnostic targets and therapeutic agents...

...tissues). Administration of L-asparaginase enzymatically catalyzes the hydrolysis of asparagine to aspartic acid and ammonia , which deprives the malignant cells of the asparagine from extracellular fluid and eventually results in...ii) it has the ability to regulate the cellular levels of asparagine, aspartic acid and ammonia ;

[...

...effect of the expression of the mutant on the 26443 or 46873 substrate can be detected , e.g., by measuring fatty the amount of asparagine and/or aspartic acid and ammonia . Plasmid DNA can then be recovered from the cells that score for inhibition, or alternatively...wild type protein (e.g., altered cellular levels of asparagine and/or aspartic acid and ammonia). Moreover, the anti-26443 or -46873 antibodies of the invention can be used to detect and isolate 26443 or 46873 proteins, regulate the bioavailability of 26443 or 46873 proteins, and...from biotin-NHS(N-hydroxy-succinimide) using techniques known in the art (e.g., biotinylation kit , Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates...for detecting the presence of 26443 or 46873 in a biological sample. For example, the kit can include a compound or agent capable of detecting 26443 or 46873 protein or mRNA...

...and a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect 26443 or 46873 protein or nucleic acid...

...0327] For antibody-based kits, the kit can include: (1) a first antibody (e.g., attached to a solid support) which binds...

...0328] For oligonucleotide-based kits, the kit can include: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a...

...useful for amplifying a nucleic acid molecule corresponding to a marker of the invention. The kit can also includes a buffering agent, a preservative, or a protein-stabilizing agent. The kit can also includes components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples that can be assayed and compared to the test sample contained. Each component of the kit can be enclosed within an

individual container and all of the various containers can be...

...single package, along with instructions for interpreting the results of the assays performed using the kit .

[...solid support, e.g., to different addresses of an array or to different beads or nanoparticles .

[

Non-exemplary or Dependent Claim(s):

...11. A kit comprising a compound which selectively binds to a polypeptide of claim 5 and instructions for...

...14. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and...

3/3,KWIC/17 (Item 9 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

0005780441

Derwent Accession: 2004-071254

Compositions and methods for liver growth and liver protection

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	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	----	-----	-----
Main Patent	US 20040170613	A1	20040902	US 2003455470	20030605
Provisional				US 60-386637	20020605

Fulltext Word Count: 27278

Summary of the Invention:

...0034] An article of manufacture and a kit comprising a VEGFR modulating agent are also provided

Description of the Invention:

...markers include, procollagen type III peptide levels (PIIIP) to assess if hepatic fibrogenesis is active; ammonia blood levels in hepatoencephalopathies; ligand in levels in necrosis and hepatoma; hyaluronate levels due to hepatic endothelial cell damage; a-1-fetoprotein (AFP) levels to detect hepatoma; carcinoembryonic antigen (CEA) levels to detect cancer metastasis to the liver; elevations of antibodies...

...techniques or by interfacial polymerization, in colloidal drug delivery systems (e.g., liposomes, microspheres, microemulsions, nanoparticles and nanocapsules), or in macroemulsions. Such techniques are known in the art and disclosed in...

...0149] The invention also provides a pharmaceutical pack or kit

comprising one or more containers filled with one or more of the ingredients of the...Greek]m cell strainer (Falcon, Bedford, Mass.). For BrdU staining, the in situ Cell Proliferation Kit was used according to the manufacturer's recommendations (Roche Molecular Biochemicals, Indianapolis, Ind.). In short...

...degree C. Immunoreactivities were visualized by the avidin-biotin complex technique using Vectastain Elite ABC kit (Vector Laboratories, Burlingame, Calif.) with diaminobenzidine as chromogen. Hematoxylin was used as counterstain. BrdU immunohistochemistry...

...were washed twice in ice cold PBS and total RNA was isolated using the RNeasy kit (Qiagen) according to the instructions of the manufacturer. Fifty ng of total RNA per reaction were analyzed using the RT-PCR kit from Perkin-Elmer, following the manufacturer's instructions (PE Applied Biosystems, Foster City, Calif.). Reactions...

...Adenovirus stocks were further amplified in HEK293 cells and purified using the Virakit Adeno purification kit (Virapur, Carlsbad, Calif.). Adenovirus titers were obtained by agarose-overlayed plaque assays...

...0194] Adenovirus was directly injected into the tail vein of mice. Virus was stored in Kit Formulation Buffer supplied by Virapur and the appropriate dilutions were made with PBS. The volume...

Exemplary or Independent Claim(s):

...79. A kit comprising: a) a first container, a label on said first container, and a composition contained...

...a second container comprising a pharmaceutically acceptable buffer; and c) an instruction for using the kit for promoting liver growth.

Non-exemplary or Dependent Claim(s):

...the polymer matrix is a microcapsule selected from the group consisting of liposome, microsphere, microemulsion, **nanoparticle** and nanocapsule...

...the polymer matrix is a microcapsule selected from the group consisting of liposome, microsphere, microemulsion, **nanoparticle** and nanocapsule...

...the polymer matrix is a microcapsule selected from the group consisting of liposome, microsphere, microemulsion, **nanoparticle** and nanocapsule...

...the polymer matrix is a microcapsule selected from the group consisting of liposome, microsphere, microemulsion, **nanoparticle** and nanocapsule...

3/3,KWIC/18 (Item 10 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005687084 **IMAGE Available
Derwent Accession: 2004-180269
Method and composition for inhibiting cancer cell growth
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McElroy, Jerry, INV
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Wong, Wah, INV

Docherty, John, INV
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040115186	A1	20040617	US 2003621833	20030716
Provisional				US 60-397244	20020718

Fulltext Word Count: 32519

Summary of the Invention:

...0021] Also disclosed is a kit for use in inhibiting growth of cancer cells in a mammalian subject. The kit has a pharmaceutical composition containing urease enzyme, and instructional materials teaching the administration of the...

Description of the Invention:

...Greek[m] may be designed using polymers able to be degraded in vivo. Biodegradable polyisobutylcyanoacrylate nanoparticles that meet these requirements are contemplated for use in the present invention, and such particles...

...2001) Int J Pharm 214(1-2):13-6. Methods of preparing polyalkyl-cyano-acrylate nanoparticles containing biologically active substances and their use are described in U.S. Pat. Nos. 4...and diagnosis of various cancer types. Kits, as described below, are also contemplated, wherein the kit comprises a dosage form of a pharmaceutical composition and a package insert containing instructions for...effective to reach the tumor site. The urease hydrolyzes the labelled urea to produce labelled ammonia, which could be detected on the scan...

...the use of active agents for inhibiting tumor cell growth. Thus, in one embodiment, the kit includes a pharmaceutical composition containing an active agent, preferably a urease enzyme, and instructional materials...

Exemplary or Independent Claim(s):

...44. A kit for use in inhibiting growth of cancer cells in a mammalian subject, said kit comprising a pharmaceutical composition containing urease enzyme, and instructional materials teaching the administration of the...

Non-exemplary or Dependent Claim(s):

...45. The kit of claim 44, wherein said instructional material teaches administering the urease composition to a subject...

...46. The kit of claim 44, wherein said instructional material teaches administering the urease composition to a subject...

...47. The kit of claim 44, wherein said instructional material teaches administering the urease composition to a subject...

3/3,KWIC/19 (Item 11 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005457615 **IMAGE Available

Derwent Accession: 2003-210159

Chimeric immunomodulatory compounds and methods of using the same - III

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20030225016	A1	20031204	US 2002328578	20021223
CIP	PENDING			US 2002176883	20020621
CIP	PENDING			US 2002177826	20020621
Provisional				US 60-299883	20010621
Provisional				US 60-375253	20020423
Provisional				US 60-299883	20010621
Provisional				US 60-375253	20020423

Fulltext Word Count: 58894

Description of the Invention:

...progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether **detectable** or undetectable. "Treatment" can also mean prolonging survival as compared to expected survival if not...a CIC and antigen are coadministered by adsorbing both to a surface, such as a **nanoparticle** or microcarrier. Adsorption of a CIC and/or antigen to a surface may occur through...

...0396] In general, characteristics of **nanoparticles**, such as surface charge, particle size and molecular weight, depend upon polymerization conditions, monomer concentration...

...with an antigen preparation, for example, in the form of a lipid-antigen mixture. Such **nanoparticles** are self-assembling complexes of nanometer sized particles, typically on the order of 0.1...

...0398] Another adsorbent surface are **nanoparticles** made by the polymerization of alkylcyanoacrylates. Alkylcyanoacrylates can be polymerized in acidified aqueous media by...

...sizes in the range of 20 to 3000 nm, and it is possible to make **nanoparticles** specific surface characteristics and with specific surface charges (Douglas et al., 1987, supra). For example, oligonucleotides may be adsorbed to polyisobutyl- and polyisohexylcyanoacrylate **nanoparticles** in the presence of hydrophobic cations such as tetraphenylphosphonium chloride or quaternary ammonium salts, such as cetyltrimethyl ammonium bromide. Oligonucleotide adsorption on these **nanoparticles** appears to be mediated by the formation of ion pairs between negatively charged phosphate groups...

...et al. (1992) Pharm. Res. 9:441-449. Polypeptides may also be adsorbed to polyalkylcyanoacrylate **nanoparticles**. See, for example, Douglas et al., 1987; Schroeder et al. (1998) Peptides 19:777-780...

...0399] Another adsorbent surface are **nanoparticles** made by the polymerization of methylenemalonate. For example, as described in Bousquet et al., 1999, polypeptides adsorbed to poly(methylenemalonate 2.1.2) **nanoparticles** appear to do so initially through electrostatic forces followed by stabilization through hydrophobic forces...scratch the

outermost layer of epidermal cells. Each of the tines in the MONO-VACC kit is coated with old tuberculin; in the present invention, each needle is coated with a...instructions on a label or package insert (e.g., a paper sheet included in the kit), but machine-readable instructions (e.g., instructions carried on a magnetic or optical storage disk...

...or more containers including materials for producing liquid phase MC. For example, a CIC/MC kit for oil-in-water emulsion MC may comprise one or more containers containing an oil...

3/3,KWIC/20 (Item 12 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005220877 **IMAGE Available
Derwent Accession: 2002-075167

Production of polyketides

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20030073205	A1	20030417	US 2001957483	20010919
Provisional				US 60-232696	20000914
Provisional				US 60-257517	20001221
Provisional				US 60-269020	20010213
Priority				WO 2001US13793	20010426

Fulltext Word Count: 59414

Description of the Invention:

...0339] Where applicable, the inventive compounds may be formulated as microcapsules and nanoparticles . General protocols are described for example, by Microcapsules and Nanoparticles in Medicine and Pharmacy by Max Donbrow, ed., CRC Press (1992) and by U.S...cells are embedded in agarose and lysed according to the BIO-RAD genomic DNA plug kit . DNA plugs are partially digested with restriction enzyme, such as Sau3AI or HindIII, and electrophoresed...

...for 5 min. The supernatant was then used for ammonia analysis with an ammonia assay kit (Sigma). Samples were diluted 20-100 fold with water until the final concentrations were less...

...With the consumption of casitone by the cells, a gradual accumulation of ammonium was also detected in the production medium. The final ammonia concentration approached 20 mM at the end of the 5-day fermentation...

broth is clarified by centrifugation in a microcentrifuge (5 minutes, 12000 rpm). An ammonia assay kit from Sigma (Catalog #171-UV) is used for quantitation, with the clarified fermentation broth substituted in place of the blood plasma described in the kit protocol. As the linear response range of this colorimetric assay is only 0.01176-0...

3/3,KWIC/21 (Item 13 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005061213 **IMAGE Available
Derwent Accession: 2000-256506

ELECTROTRANSORT DEVICE COMPRISING BLADES

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020115957	A1	20020822	US 99385284	19990830
Provisional				US 60-98494	19980831
Provisional				US 60-129705	19990416

Fulltext Word Count: 15012

Description of the Invention:

...carboxylic acid functional groups; the concentration of gases, such as oxygen, hydrogen, carbon dioxide, and ammonia ; color; viscosity; density; temperature; pressure; and the concentration of reactants and products of oxidation and reduction processes on electrodes. Examples of such sensors include, but are not limited to, conductivity sensors; impedance sensors; ion-selective electrodes, such as...

...following: (a) liposomes; (b) cyclodextrins; (c) micelles; (d) microcapsules; (e) microemulsions; (f) hydrogels; and (g) nanoparticles

[...]

...lysine double-coated slides. The tissue sections were then processed using a Histostain-SP DAB kit (Zymed Laboratories, Inc., Burlingame, Calif.) according to the manufacture's recommendations. The sections were treated

3/3,KWIC/22 (Item 14 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0004983392 **IMAGE Available
Derwent Accession: 2002-329129

C/ 26443 and 46837, novel human asparaginase family members and uses therefor

; AS REAGENTS OR TARGETS IN ASSAYS APPLICABLE TO TREATMENT AND DIAGNOSIS

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 Unassigned Or Assigned To Individual (Code: 68000)

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020038014	A1	20020328	US 2001816664	20010323
Provisional				US 60-191973	20000324
Provisional				US 60-191973	20000324

Fulltext Word Count: 45215

Description of the Drawings:

...effect of the expression of the mutant on the 26443 or 46873 substrate can be **detected**, e.g., by measuring fatty the amount of asparagine and/or aspartic acid and **ammonia**. Plasmid DNA can then be recovered from the cells that score for inhibition, or alternatively...

...wild type protein (e.g., altered cellular levels of asparagine and/or aspartic acid and **ammonia**). Moreover, the anti-26443 or -46873 antibodies of the invention can be used to **detect** and isolate 26443 or 46873 proteins, regulate the bioavailability of 26443 or 46873 proteins, and...from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates...for detecting the presence of 26443 or 46873 in a biological sample. For example, the kit can include a compound or agent capable of detecting 26443 or 46873 protein or mRNA...

...and a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect 26443 or 46873 protein or nucleic acid...

...0280] For antibody-based kits, the kit can include: (1) a first antibody (e.g., attached to a solid support) which binds...

...0281] For oligonucleotide-based kits, the kit can include: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a...

...useful for amplifying a nucleic acid molecule corresponding to a marker of the invention. The kit can also includes a buffering agent, a preservative, or a protein-stabilizing agent. The kit can also includes components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples that can be assayed and compared to the test sample contained. Each component of the kit can be enclosed within an individual container and all of the various containers can be...

...single package, along with instructions for interpreting the results of the assays performed using the kit.

[...solid support, e.g., to different addresses of an array or to different beads or **nanoparticles**.

[

Description of the Invention:

...be used. The DNA was radioactively labeled with [sup]32P-dCTP using the Prime-It Kit (Stratagene, La Jolla, Calif.) according to the instructions of the supplier. Filters containing mRNA from...

Non-exemplary or Dependent Claim(s):

...15. A kit comprising a compound that selectively binds to a polypeptide of claim 8 and instructions for...

...18. A kit comprising a compound that selectively hybridizes to a nucleic acid molecule of claim 1 and...

3/3,KWIC/23 (Item 15 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

4838888 **IMAGE Available

Derwent Accession: 2000-256506

Utility

E/ Electrotransort device comprising blades

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Oakeson, Ralph W., Somerville, NJ

Wisniewski, Stephen J., Doylestown, PA

Wang, Jonas C. T., West Windsor, NJ

Niemiec, Susan M., Yardley, PA

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Johnson & Johnson Consumer Cos Inc (Code: 56111)

Examiner: Mendez, Manuel (Art Unit: 323)

Combined Principal Attorneys: McGowan, William E.

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6532386	A	20030311	US 99385284	19990830

Fulltext Word Count: 13584

Description of the Invention:

...carboxylic acid functional groups; the concentration of gases, such as oxygen, hydrogen, carbon dioxide, and ammonia; color; viscosity; density; temperature; pressure; and the concentration of reactants and products of oxidation and reduction processes on electrodes. Examples of such sensors include, but are not limited to, conductivity sensors; impedance sensors; ion-selective electrodes, such as...

...following: (a) liposomes; (b) cyclodextrins; (c) micelles; (d) microcapsules; (e) microemulsions; (f) hydrogels; and (g) nanoparticles

...

...lysine double-coated slides. The tissue sections were then processed using a Histostain-SP DAB kit (Zymed
? ds

Set	Items	Description
S1	118	(AMMONIA? (25N) (DETECT? OR SENSOR?)) AND NANOPARTIC?
S2	114	RD (unique items)
S3	23	S2 AND KIT
?		

? s s2 not s3

114 S2

23 S3

S4 91 S2 NOT S3

? t s4/3,kwic/all

4/3,KWIC/1 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

15262213 PMID: 15712880

[Primary study on determination of the size distribution of nanoparticles by capillary zone electrophoresis]

Xue Yan; Yang Haiying; Yang Yongtan

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Se pu = Chinese journal of chromatography / Zhongguo hua xue hui (China)

Mar 2004, 22 (2) p170-3, ISSN 1000-8713--Print Journal Code: 9424804

Publishing Model Print

Document type: Journal Article ; English Abstract

Languages: CHINESE

Main Citation Owner: NLM

Record type: MEDLINE; Completed

[Primary study on determination of the size distribution of nanoparticles by capillary zone electrophoresis]

... conditions were as follows: 8.00 mmol/L NaH₂PO₄ (adjusted to pH 8.00 with ammonia) as buffer, applied voltage of 26 kV and detection wavelength of 214 nm. The relative standard deviation of the migration time and the peak...

4/3,KWIC/2 (Item 2 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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12499520 PMID: 10444842

Evaluation of volatile eluents and electrolytes for high-performance liquid chromatography-electrospray ionization mass spectrometry and capillary electrophoresis-electrospray ionization mass spectrometry of proteins. II. Capillary electrophoresis.

Huber C G; Premstaller A; Kleindienst G

Institute of Analytical Chemistry and Radiochemistry, Leopold-Franzens-University, Innsbruck, Austria. christian.huber@uibk.ac.at

Journal of chromatography. A (NETHERLANDS) Jul 16 1999, 849 (1)

p175-89, ISSN 0021-9673--Print Journal Code: 9318488

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Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... electrophoresis (CE) in fused-silica capillaries coated with an irreversibly adsorbed monolayer of derivatized polystyrene nanoparticles . Whereas phosphate buffer, pH 3.10, enabled the highly efficient separation of basic proteins with...

... fmol amounts of proteins during coupled CE-ESI-MS utilizing 100-125 mM formic acid- ammonia , pH 3.10. However, compared to UV detection , considerable band broadening is observed with ESI-MS detection which is

mainly attributed to column overloading, band spreading in the interface, and scanning data...

4/3,KWIC/3 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01172459

Nanoparticle structure for use in an electronic device, especially in a chemical sensor

Nanoteilchenstruktur zur Anwendung in einer elektronischen Anordnung, insbesondere in einem chemischen Sensor

Structure nanoparticulaire a utiliser dans un dispositif electronique, en particulier dans un capteur chimique

PATENT ASSIGNEE:

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PATENT (CC, No, Kind, Date): EP 1022560 A1 000726 (Basic)
EP 1022560 B1 041222

APPLICATION (CC, No, Date): EP 99101141 990121;

DESIGNATED STATES: DE; FR; GB

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS (V7): G01N-027/12; H01L-051/20

ABSTRACT WORD COUNT: 87

NOTE:

Figure number on first page: 2

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200030	687
CLAIMS B	(English)	200452	856
CLAIMS B	(German)	200452	824
CLAIMS B	(French)	200452	881
SPEC A	(English)	200030	2913
SPEC B	(English)	200452	2999
Total word count - document A			3601
Total word count - document B			5560
Total word count - documents A + B			9161

Nanoparticle structure for use in an electronic device, especially in a chemical sensor

Structure nanoparticulaire a utiliser dans un dispositif electronique, en particulier dans un capteur chimique

...ABSTRACT A1

The invention relates to an electronic device comprising a nanoparticle structure and configured such that, when driven by a power source, a current path is defined through said nanoparticle structure, wherein the nanoparticle structure comprises a substrate and metal and/or semiconductor nanoparticles, wherein the nanoparticles are linked to each other and/or to the substrate by bifunctional or polyfunctional ligands...

...SPECIFICATION W. Snow, Anal. Chem. 1998, 70, 2856 proposed a new type of sensor, comprising gold **nanoparticles** deposited on a quartz substrate comprising a microelectrode structure. The **nanoparticles** were deposited on the substrate by spraying (airbrush technique). The conductivity of the **nanoparticle** layer changed with the concentration of toluene vapour in the surrounding atmosphere and allowed a...

...It is the object of the present invention to provide an electronic device comprising a **nanoparticle** structure, which is especially suitable for use as a sensor and which can be more...

...of an analytic process.

This object is accomplished by an electronic device which comprises a **nanoparticle** structure and is configured such that a current can be conducted through said **nanoparticle** structure, and which is characterized in that the **nanoparticle** structure comprises a substrate and semiconductor and/or metal **nanoparticles**, wherein the **nanoparticles** are linked to each other and/or to the substrate by bifunctional or polyfunctional ligands...

...semiconductor. The latter is preferred if the device is used in an integrated structure. The **nanoparticles** preferably are made of good conductors. In order to provide chemical stability it is preferred...

...preferred. The function of the bifunctional or polyfunctional ligands is to connect two or more **nanoparticles** so that a structure is formed that is both mechanically and electrochemically stabilized.

In a preferred embodiment of the invention the **nanoparticles** are arranged in layers, wherein **nanoparticles** in each of said layers and **nanoparticles** of adjacent layers are interconnected by one or more of said ligands.

Preferably, the ligands interconnecting the **nanoparticles** are basically of the same length, although it may also be envisaged to use ligands of different lengths, for example connecting layers and for connecting **nanoparticles** within one layer, respectively.

In a preferred embodiment it is provided that said ligands comprise...

...or inorganic compounds may be used as linkers (ligands).

According to a specific embodiment, the **nanoparticle** structure is integrated together with a transistor structure to form a controlling element for current...

...out above, wherein a (resonant) tunneling structure is formed by one or more layers of **nanoparticles** sandwiched between insulating barriers and this tunneling structure is arranged to control a transistor by...

...or gas phase, wherein the analyte is detected by a change of conductivity of the **nanoparticle** structure.

Furthermore, the invention provides a sensor for detecting one or more analytes in a...

...gas phase, especially a sensor forming an electronic device as set out previously, comprising a **nanoparticle** structure, which is accessible to an analyte in the environment of the sensor, and means for detecting the conductivity of said **nanoparticle** layer, characterized in that the **nanoparticle** structure comprises a substrate and semiconductor and/or metal **nanoparticles**, wherein the **nanoparticles** are linked with each other and/or the substrate by bifunctional or polyfunctional ligands.

Preferably the means for detecting the conductivity of said **nanoparticle** layer work according to an electric measurement principle,

i.e. they detect the current flowing...

...used. Although this is the preferred embodiment, other ways for detecting the conductivity of the nanoparticle layer and related means could be contemplated for use in the sensor according to the...

...optically determining the conductivity, e.g. by optically measuring the complex dielectric function of the nanoparticle structure.

The invention may especially provide that the ligands define cavities having a size greater...

...said analyte.

Furthermore, the invention may provide that the surface of at least of some nanoparticles is modified to favour adsorption of a specific analyte and/or hinder or prevent adsorption of substances other than said analyte.

The invention especially applies to a sensor that it is adapted to detect one or more of the following substances: ammonia, ethanol, propanol, water, aliphatic and aromatic hydrocarbons.

According to a specific embodiment of the invention it may be provided that the sensor comprises an amplifying element controlled by the current flowing through the nanoparticle structure.

Especially, the nanoparticle structure may be arranged such that it controls the base current of a bipolar transistor through changes of its conductivity.

Furthermore, it can be provided that the nanoparticle structure is enclosed between two tunneling barriers and forms a resonant tunneling device controlling the amplifying element.

Preferably the nanoparticle structure is integrated together with said amplifying element in an integrated circuit (IC).

According to a specific embodiment, a chemically selective membrane is provided on top of the nanoparticle structure so that it is exposed to the analyte, or within the nanoparticle structure.

The invention also provides an advantageous method to produce a nanoparticle structure for use in devices in sensors as described above, which are characterized in that...

...Especially, such a method may comprise the following steps:

a) linking a first layer of nanoparticles to a substrate by ligand molecules,

b) linking bifunctional or polyfunctional ligands to said first layer of nanoparticles,

c) linking a further layer of nanoparticles to said bifunctional or polyfunctional ligands, wherein steps b) and c) may be repeated to create a plurality of stacked nanoparticle monolayers on said substrate.

Preferably, the nanoparticle layers are essentially monolayers.

Preferably the entire nanoparticle structure has a thickness in the range of 50 to 100 nm. In the preferred embodiments, the nanoparticle structure comprises about 10 to 20 layers.

The term "nanoparticle", as used in the context of this application, is to be understood as a particle...

...using bifunctional or polyfunctional ligands it is also possible to define the location of the nanoparticles with regard to each other and to the substrate in a much more precise manner...

...adjusting the size of the ligands and thus the size of the cavities between the nanoparticles, the size of these cavities can be adjusted to fit the size of an analyte...

...possible to promote the selectivity by providing the ligands and/or the

surface of the **nanoparticles** with desirable chemical properties favouring the adsorption of the analyte and preventing or hindering the adsorption of undesired substances. The new **nanoparticle** structure according to the invention is not only useful for sensors, but also for producing...

...comprise a resonant tunneling transistor, wherein the tunneling element is formed by at least one **nanoparticle** structure between two insulating barriers. Resonant tunneling transistors are described, for example, in Michael S...

...made by conventional techniques, e.g. employing semiconductors, by a resonant tunneling device comprising a **nanoparticle** structure having tunneling barriers on both sides. Especially referring to such resonant tunneling transistors, it should be understood that the present application is not limited to transistors having a **nanoparticle** structure comprising bifunctional or polyfunctional ligands and rather comprises also embodiments wherein the **nanoparticle** structure is of a different nature.

Further features and advantages of the present invention will...

...for use as a chemical sensor and

Fig. 2 schematically shows the nature of the **nanoparticle** structure employed according to the present invention.

In the embodiment schematically shown in Fig. 1...

...1, which may be a glass plate, a silicon wafer or the like, carrying a **nanoparticle** structure 3. On the **nanoparticle** structure there are contacts 5, 7 to be connected with a power supply 8 and a current measuring device 9 for determining the conductivity or resistance of the **nanoparticle** structure. The contacts 5 and 7 may be of any suitable form and may especially...

...these contacts is only relevant in that they should allow measuring the conductivity of the **nanoparticle** structure in a reliable way. For example, it could be envisaged to provide them on the substrate.

Fig. 2 shows the **nanoparticle** structure and its connection to the substrate schematically in more detail. On the substrate 1 a first layer I of **nanoparticles** 11 is provided, which are linked to the substrate by linking molecules or ligands 13. Suitable ligands for fixing the **nanoparticles** to a substrate are well known and available to people skilled in the art. For example, if the **nanoparticles** consist of gold and a glass substrate is used, a suitable ligand is 3-aminopropyltriethoxysilane. The **nanoparticles** 11 of layer I are also linked with each other through ligands 15, which are preferably different from the ligands 13 linking the **nanoparticles** to the substrate. Such ligands may especially be mercaptoalkylsilanes, aminoalkylsilanes, dimercaptoalkanes, diaminoalkanes or polyfunctionalized polymers.

Overlying the first layer of **nanoparticles** there is a second layer II of **nanoparticles** 11 which are linked to the **nanoparticles** of the first layer I by said ligands 15 and also linked with each other...

...I. On the second layer, there may be one or more further layers (III) of **nanoparticles** which are interlinked within the layer and to the layer below in the manner previously described. Preferably, in order to allow an easy diffusion of analytes, the **nanoparticle** layer should be thin, but thick enough to allow a conductivity in a range that can be readily detected. A presently preferred range for the thickness of the **nanoparticle** structure is about 50 to 100 nm.

In order to improve the selectivity of the sensor, a selective membrane may be arranged on top of the uppermost **nanoparticle** layer or embedded in the **nanoparticle** structure. Such membranes may be manufactured in a

variety of manners, especially by molecular imprinting...

...1998, 10, 149), which also allow to implement a selective membrane or structure within the **nanoparticle** structure.

From Fig. 2 it can be seen that the ligands connecting **nanoparticles** 11 define cavities into which analyte molecules 17 may diffuse. If analyte molecules occupy these cavities, the conductivity of the **nanoparticle** structure changes. It was shown that the amount and direction of the change (positive or...

...analytes. Depending on the nature of the analyte and the materials used to build the **nanoparticle** structure, adsorption to the **nanoparticles** and/or to the ligands may also take place. By tailoring the size of these ...

...Furthermore, adsorption of analyte molecules may be promoted by adjusting the chemical properties of the **nanoparticles** and/or the ligands in a manner well known per se. For example, hydrophilic, hydrophobic...

...is promoted and the adsorption of undesired substances, e.g. water, is prevented.

Likewise, the **nanoparticles** may be chosen to consist of a suitable metal and/or to have a surface...

...gold or platinum, which are also chemically inert, are preferred as basic materials for the **nanoparticles** in order to get a good conductivity signal. However, other materials showing an acceptable conductivity...

...surface with linking molecules linking to the substrate and able to link to the envisaged **nanoparticles** as well. On the substrate surface thus prepared a first layer of **nanoparticles** is provided which are linked to said linking molecules. In the next step multifunctional ligands linking to the **nanoparticles** are added to which a new layer of **nanoparticles** is linked in the next step and so on so that by adding step by step **nanoparticles** and multifunctional ligands a layered structure is formed.

Example

In order to prepare a sensor according to the present invention, **nanoparticles** were prepared as described in D.V. Leff, L. Brandt, J.R. Heath, Langmuir, 1996...

...linked with each other and self-assembled by the use of 1,6-dimercaptohexane. The **nanoparticle** structure thus created consists of several layers of self-assembled **nanoparticles**. Contacts were applied and connected to a resistance measuring circuit. The sensors thus built showed...

...device towards the analytes could be adjusted by heating the structure before using as a **sensor**. For example, the response to an exposure to ammonia or water changed from an increase to a decrease of conductivity after curing it at elevated temperature. The use of a long-chain dithiolalkanes as bifunctional linkers between the **nanoparticles** improved the sensitivities towards some organic compounds.

Due to the use of **nanoparticles**, the sensor according to the invention has a high sensitivity with a high signal-to-noise ration even for low analyte concentrations. Due to the linking of the **nanoparticles**, the structure is more stable than according to the prior art. Especially, stability against humidity...

...SPECIFICATION B1

This invention relates to a **nanoparticle** structure for use in an electronic device according to the first part of claim 1...

...W. Snow, Anal. Chem. 1998, 70, 2856 proposed a new type of sensor, comprising gold **nanoparticles** deposited on a quartz substrate comprising a microelectrode structure. The **nanoparticles** were deposited on the substrate by spraying (airbrush technique). The conductivity of the **nanoparticle** layer changed with the concentration of toluene vapour in the surrounding atmosphere and allowed a...

...a single electron transistor.

It is the object of the present invention to provide a **nanoparticle** structure which is specially suitable for use in an electronic device and specially in a...

...more closely tailored to the needs of analytic porcesses.

This object is achieved by a **nanoparticle** structure according to claim 1, by the use of a sensor according to claim 11...

...semiconductor. The latter is preferred if the device is used in an integrated structure. The **nanoparticles** preferably are made of good conductors. In order to provide chemical stability it is preferred...

...preferred. The function of the bifunctional or polyfunctional ligands is to connect two or more **nanoparticles** so that a structure is formed that is both mechanically and electrochemically stabilized.

In a preferred embodiment of the invention the **nanoparticles** are arranged in layers, wherein **nanoparticles** in each of said layers and **nanoparticles** of adjacent layers are interconnected by one or more of said ligands.

Preferably, the ligands interconnecting the **nanoparticles** are basically of the same length, although it may also be envisaged to use ligands of different lengths, for example connecting layers and for connecting **nanoparticles** within one layer, respectively.

In a preferred embodiment it is provided that said ligands comprise...

...or inorganic compounds may be used as linkers (ligands).

According to a specific embodiment, the **nanoparticle** structure is integrated together with a transistor structure to form a controlling element for current...

...out above, wherein a (resonant) tunneling structure is formed by one or more layers of **nanoparticles** sandwiched between insulating barriers and this tunneling structure is arranged to control a transistor by...

...or gas phase, wherein the analyte is detected by a change of conductivity of the **nanoparticle** structure.

Furthermore, the invention provides a sensor for detecting one or more analytes in a...

...gas phase, especially a sensor forming an electronic device as set out previously, comprising a **nanoparticle** structure, which is accessible to an analyte in the environment of the sensor, and means for detecting the conductivity of said **nanoparticle** layer, characterized in that the **nanoparticle** structure comprises a substrate and semiconductor and/or metal **nanoparticles**, wherein the **nanoparticles** are linked with each other and/or the substrate by bifunctional or polyfunctional ligands.

Preferably the means for detecting the conductivity of said

nanoparticle layer work according to an electric measurement principle, i.e. they detect the current flowing...

...used. Although this is the preferred embodiment, other ways for detecting the conductivity of the nanoparticle layer and related means could be contemplated for use in the sensor according to the...
...optically determining the conductivity, e.g. by optically measuring the complex dielectric function of the nanoparticle structure.

The invention may especially provide that the ligands define cavities having a size greater...

...said analyte.

Furthermore, the invention may provide that the surface of at least of some nanoparticles is modified to favour adsorption of a specific analyte and/or hinder or prevent adsorption of substances other than said analyte.

The invention especially applies to a sensor that it is adapted to detect one or more of the following substances: ammonia, ethanol, propanol, water, aliphatic and aromatic hydrocarbons.

According to a specific embodiment of the invention it may be provided that the sensor comprises an amplifying element controlled by the current flowing through the nanoparticle structure.

Especially, the nanoparticle structure may be arranged such that it controls the base current of a bipolar transistor through changes of its conductivity.

Furthermore, it can be provided that the nanoparticle structure is enclosed between two tunneling barriers and forms a resonant tunneling device controlling the amplifying element.

Preferably the nanoparticle structure is integrated together with said amplifying element in an integrated circuit (IC).

According to a specific embodiment, a chemically selective membrane is provided on top of the nanoparticle structure so that it is exposed to the analyte, or within the nanoparticle structure.

The invention also provides an advantageous method to produce a nanoparticle structure for use in devices and/or in sensors as described above, which are characterized...

...Especially, such a method may comprise the following steps:

a) linking a first layer of nanoparticles to a substrate by ligand molecules,

b) linking bifunctional or polyfunctional ligands to said first layer of nanoparticles,

c) linking a further layer of nanoparticles to said bifunctional or polyfunctional ligands, wherein steps b) and c) may be repeated to create a plurality of stacked nanoparticle monolayers on said substrate.

Preferably, the nanoparticle layers are essentially monolayers.

Preferably the entire nanoparticle structure has a thickness in the range of 50 to 100 nm. In the preferred embodiments, the nanoparticle structure comprises about 10 to 20 layers.

The term "nanoparticle", as used in the context of this application, is to be understood as a particle...

...using bifunctional or polyfunctional ligands it is also possible to define the location of the nanoparticles with regard to each other and to the substrate in a much more precise manner...

...adjusting the size of the ligands and thus the size of the cavities between the nanoparticles, the size of these cavities can be adjusted to fit the size of an analyte...

...possible to promote the selectivity by providing the ligands and/or the surface of the **nanoparticles** with desirable chemical properties favouring the adsorption of the analyte and preventing or hindering the adsorption of undesired substances. The new **nanoparticle** structure according to the invention is not only useful for sensors, but also for producing...

...comprise a resonant tunneling transistor, wherein the tunneling element is formed by at least one **nanoparticle** structure between two insulating barriers. Resonant tunneling transistors are described, for example, in Michael S...

...made by conventional techniques, e.g. employing semiconductors, by a resonant tunneling device comprising a **nanoparticle** structure having tunneling barriers on both sides.

Further features and advantages of the present invention...

...for use as a chemical sensor and

Fig. 2 schematically shows the nature of the **nanoparticle** structure employed according to the present invention.

In the embodiment schematically shown in Fig. 1...

...1, which may be a glass plate, a silicon wafer or the like, carrying a **nanoparticle** structure 3. On the **nanoparticle** structure there are contacts 5, 7 to be connected with a power supply 8 and a current measuring device 9 for determining the conductivity or resistance of the **nanoparticle** structure. The contacts 5 and 7 may be of any suitable form and may especially...

...these contacts is only relevant in that they should allow measuring the conductivity of the **nanoparticle** structure in a reliable way. For example, it could be envisaged to provide them on the substrate.

Fig. 2 shows the **nanoparticle** structure and its connection to the substrate schematically in more detail. On the substrate 1 a first layer I of **nanoparticles** 11 is provided, which are linked to the substrate by linking molecules or ligands 13. Suitable ligands for fixing the **nanoparticles** to a substrate are well known and available to people skilled in the art. For example, if the **nanoparticles** consist of gold and a glass substrate is used, a suitable ligand is 3-aminopropyltriethoxysilane. The **nanoparticles** 11 of layer I are also linked with each other through ligands 15, which are preferably different from the ligands 13 linking the **nanoparticles** to the substrate. Such ligands may especially be mercaptoalkylsilanes, aminoalkylsilanes, dimercaptoalkanes, diaminoalkanes or polyfunctionalized polymers.

Overlying the first layer of **nanoparticles** there is a second layer II of **nanoparticles** 11 which are linked to the **nanoparticles** of the first layer I by said ligands 15 and also linked with each other...

...I. On the second layer, there may be one or more further layers (III) of **nanoparticles** which are interlinked within the layer and to the layer below in the manner previously described. Preferably, in order to allow an easy diffusion of analytes, the **nanoparticle** layer should be thin, but thick enough to allow a conductivity in a range that can be readily detected. A presently preferred range for the thickness of the **nanoparticle** structure is about 50 to 100 nm.

In order to improve the selectivity of the sensor, a selective membrane may be arranged on top of the uppermost **nanoparticle** layer or embedded in the **nanoparticle** structure. Such membranes may be manufactured in a variety of manners, especially by molecular imprinting...

...1998, 10, 149), which also allow to implement a selective membrane or

structure within the nanoparticle structure.

From Fig. 2 it can be seen that the ligands connecting nanoparticles 11 define cavities into which analyte molecules 17 may diffuse. If analyte molecules occupy these cavities, the conductivity of the nanoparticle structure changes. It was shown that the amount and direction of the change (positive or...

...analytes. Depending on the nature of the analyte and the materials used to build the nanoparticle structure, adsorption to the nanoparticles and/or to the ligands may also take place. By tailoring the size of these ...

...Furthermore, adsorption of analyte molecules may be promoted by adjusting the chemical properties of the nanoparticles and/or the ligands in a manner well known per se. For example, hydrophilic, hydrophobic...

...is promoted and the adsorption of undesired substances, e.g. water, is prevented.

Likewise, the nanoparticles may be chosen to consist of a suitable metal and/or to have a surface...

...gold or platinum, which are also chemically inert, are preferred as basic materials for the nanoparticles in order to get a good conductivity signal. However, other materials showing an acceptable conductivity...

...surface with linking molecules linking to the substrate and able to link to the envisaged nanoparticles as well. On the substrate surface thus prepared a first layer of nanoparticles is provided which are linked to said linking molecules. In the next step multifunctional ligands linking to the nanoparticles are added to which a new layer of nanoparticles is linked in the next step and so on so that by adding step by step nanoparticles and multifunctional ligands a layered structure is formed.

Example

In order to prepare a sensor according to the present invention, nanoparticles were prepared as described in D.V. Leff, L. Brandt, J.R. Heath, Langmuir, 1996...

...linked with each other and self-assembled by the use of 1,6-dimercaptohexane. The nanoparticle structure thus created consists of several layers of self-assembled nanoparticles. Contacts were applied and connected to a resistance measuring circuit. The sensors thus built showed...

...device towards the analytes could be adjusted by heating the structure before using as a sensor. For example, the response to an exposure to ammonia or water changed from an increase to a decrease of conductivity after curing it at elevated temperature. The use of a long-chain dithiolalkanes as bifunctional linkers between the nanoparticles improved the sensitivities towards some organic compounds.

Due to the use of nanoparticles, the sensor according to the invention has a high sensitivity with a high signal-to-noise ration even for low analyte concentrations. Due to the linking of the nanoparticles, the structure is more stable than according to the prior art. Especially, stability against humidity...

CLAIMS 1. Electronic device which comprises a nanoparticle structure and

is configured such that a current can be conducted through said nanoparticle structure,

characterized in that the nanoparticle structure comprises a substrate and metal and/or semiconductor nanoparticles, wherein the nanoparticles are linked to each other and/or to the substrate by bifunctional or polyfunctional ligands.

2. Electronic device according to claim 1, characterized in that the nanoparticles are arranged in layers, wherein nanoparticles in each of said layers and nanoparticles of adjacent layers are interconnected by one or more of said ligands.
3. Electronic device...

...5. Electronic device according to one of claims 1 to 4, characterized in that the nanoparticle structure is integrated together with a transistor structure to form a controlling element for current...

...characterized in that a resonant tunneling structure is formed by one or more layers of nanoparticles sandwiched between insulating barriers and that this tunneling structure is arranged to control a transistor ...

...sensor forming an electronic device according to one of claims 1 to 7, comprising a nanoparticle structure, which is accessible to an analyte in the environment of the sensor, and means for detecting the conductivity of said nanoparticle layer,

characterized in that the nanoparticle structure comprises a substrate and semiconductor and/or metal nanoparticles, wherein the nanoparticles are linked with each other and/or the substrate by bifunctional or polyfunctional ligands.

9...

...of claims 8 to 10, characterized in that the surface of at least of some nanoparticles is modified to favour adsorption of a specific analyte and/or hinder or prevent adsorption of substances other than said analyte.

12. Sensor according to one of claims 8 to 11, characterized in that it is adapted to detect one or more of the following substances: ammonia, ethanol, propanol, toluene, water, hexanes.
13. Sensor according to one of claims 8 to 12, characterized in that it comprises an amplifying element controlled by the current flowing through the nanoparticle structure.
14. Sensor according to claim 13, characterized in that the nanoparticle structure is arranged such that it controls the base current of a bipolar transistor through...

...conductivity.

15. Sensor according to one of claims 13 or 14, characterized in that the nanoparticle structure is enclosed between two tunneling barriers and forms a resonant tunneling device.
16. Sensor according to one of claims 13 to 15, characterized in that the nanoparticle structure is integrated together with said amplifying element in an integrated circuit (IC).
17. Sensor...

...characterized in that a chemically selective membrane is provided on top of or within the nanoparticle structure.

18. Method for producing a nanoparticle structure for use in an electronic device according to one of claims 1 to 7...

...claims 8 to 17, characterized by the following steps:

- a) linking a first layer of **nanoparticles** to a substrate by ligand molecules,
 - b) linking bifunctional or polyfunctional ligands to said first layer of **nanoparticles**,
 - c) linking a further layer of **nanoparticles** to said bifunctional or polyfunctional ligands.
19. Method according to claim 18, characterized in that steps b) and c) are repeated to create a plurality of stacked **nanoparticle** monolayers on said substrate.

...CLAIMS B1

1. **Nanoparticle** structure for use in an electronic device configured such that a current can be conducted through said **nanoparticle** structure (3),

the **nanoparticle** structure (3) comprising a substrate (1) and metal and/or semiconductor **nanoparticles** (11), wherein the **nanoparticles** (11) are linked to each other and/or to the substrate (1) by bifunctional or...

...cavities having a size greater or equal to that of a molecule diffusing therein.

2. **Nanoparticle** structure according to claim 1, characterized in that molecules diffusing into said cavities are of one or more of the following substances: ammonia, ethanol, propanol, toluene, water, hexanes.
3. **Nanoparticle** structure according to claim 1 or 2, characterized in that the **nanoparticles** (11) are arranged in layers, wherein **nanoparticles** (11) in each of said layers and **nanoparticles** (11) of adjacent layers are interconnected by one or more of said ligands (15).
4. **Nanoparticle** structure according to one of claims 1 to 3, characterized in that said ligands (13, 15) comprise one or more amino groups and/or one or more thiol groups.
5. **Nanoparticle** structure according to one of claims 1 to 4, characterized in that the ligands (13...

...are chosen from the group comprising mercaptoalkylsilanes, aminoalkylsilanes, dimercaptoalkanes, dithiolalkanes, diaminoalkanes, dihydroxylalkanes and dicarboxylalkanes.

6. **Nanoparticle** structure according to one of claims 1 to 5, characterized in that the **nanoparticle** structure (3) is integrated together with a transistor structure to form a controlling element for current between terminals of the transistor.
7. **Nanoparticle** structure according to claim 6, characterized in that a resonant tunneling structure is formed by one or more layers of **nanoparticles** (13, 15) sandwiched between insulating barriers and that this tunneling structure is arranged to control...

...current flowing therethrough in response to a voltage applied to the resonant tunneling structure.

8. **Nanoparticle** structure according to one of claims 1 to 7, characterized in that the ligands (13...

...and/or to prevent or hinder the adsorption of substances other than said analyte.

9. **Nanoparticle** structure according to one of claims 1 to 8, characterized in that the surface of at least of some **nanoparticles**

- (11) is modified to favour adsorption of a specific analyte and/or hinder or prevent adsorption of substances other than said analyte.
10. Use of a **nanoparticle** structure according to one of claims 1 to 9 as a sensor for selectively detecting...
- ...Sensor for detecting one or more analytes in a liquid or gas phase, comprising a **nanoparticle** structure (3) according to claim 1 and further comprising a substrate (1) and means for detecting the conductivity of said **nanoparticle** structure (3).
12. Sensor according to claim 11, characterized in that the ligands (13, 15...
- ...to claim 11 or 12, characterized in that the surface of at least of some **nanoparticles** (11) is modified to favour adsorption of a specific analyte and/or hinder or prevent adsorption of substances other than said analyte.
14. **Sensor** according to one of claims 11 to 13, characterized in that it is adapted to **detect** one or more of the following substances: ammonia, ethanol, propanol, toluene, water, hexanes.
15. **Sensor** according to one of claims 11 to 14, characterized in that it comprises an amplifying element controlled by the current flowing through the **nanoparticle** structure (3).
16. Sensor according to claim 15, characterized in that the **nanoparticle** structure is arranged such that it controls the base current of a bipolar transistor through...
- ...conductivity.
17. Sensor according to one of claims 15 or 16, characterized in that the **nanoparticle** structure (3) is enclosed between two tunneling barriers and forms a resonant tunneling device.
18. Sensor according to one of claims 15 to 17, characterized in that the **nanoparticle** structure (3) is integrated together with said amplifying element in an integrated circuit (IC).
- 19...
- ...characterized in that a chemically selective membrane is provided on top of or within the **nanoparticle** structure.
20. Method for producing a **nanoparticle** structure according to claim 1 for use in an electronic device and/or a sensor...
- ...one of claims 11 to 19, comprising the steps:
- a) linking a first layer of **nanoparticles** (11) to a substrate (1) by ligand molecules (13);
 - b) linking bifunctional or polyfunctional ligand molecules (15) to said first layer of **nanoparticles** (11), the size of the ligand molecules (15) being adjusted such that cavities between said **nanoparticles** (11) are formed having a size permitting the analyte to be detected to diffuse into said cavities; and
 - c) linking a further layer of **nanoparticles** (11) to said bifunctional or polyfunctional ligands (15).
21. Method according to claim 20, characterized in that steps b) and c) are repeated to create a plurality of stacked **nanoparticle** monolayers on said substrate (1).
22. Method according to claim 20 or 21, characterized in that it comprises the step of modifying the surface of at least some **nanoparticles** (11) to favour adsorption of a specific analyte and/or hinder or prevent adsorption of...
- ...CLAIMS oder Verhinderung oder Behinderung der Adsorption von anderen Substanzen als dem Analyt modifiziert ist.
14. **Sensor** nach einem der Anspruche 11 bis 13, dadurch gekennzeichnet,

das er zur Detektion einer oder mehrerer der folgenden Substanzen geeignet ist: Ammoniak, Ethanol, Propanol, Toluol, Wasser, Hexan.

15. Sensor nach einem der Ansprüche 11 bis 14, dadurch gekennzeichnet, das er ein durch den durch...

...CLAIMS B1

1. Structure a nanoparticules destinee a etre utilisee dans un dispositif electronique configure de telle maniere qu'un courant peut etre etabli a travers ladite structure a nanoparticules (3), la structure a nanoparticules (3) comprenant un substrat (1) et des nanoparticules metalliques et/ou semiconductrices (11), ou les nanoparticules (11) sont liees entre elles et/ou au substrat (1) par des ligands bifonctionnels ou...

...superieure ou egale a celle d'une molecule diffusant a l'interieur.

2. Structure a nanoparticules selon la revendication 1, caracterisee en ce que les molecules diffusant dans lesdites cavites sont...

...une ou plusieurs des substances suivantes : ammoniac, ethanol, propanol, toluene, eau, hexanes.

3. Structure a nanoparticules selon la revendication 1 ou 2, caracterisee en ce que les nanoparticules (11) sont disposees en couches, ou les nanoparticules (11) dans chacune desdites couches et les nanoparticules (11) de couches adjacentes sont reliees entre elles par un ou plusieurs desdits ligands (15).

4. Structure a nanoparticules selon l'une des revendications 1 a 3, caracterisee en ce que lesdits ligands (13)...

...un ou plusieurs groupes amino et/ou un ou plusieurs groupes thiol.

5. Structure a nanoparticules selon l'une des revendications 1 a 4, caracterisee en ce que les ligands (13)...

...aminoalkylsilanes, les dimercaptoalcanes, les dithiolalcanes, les diaminoalcanes, les dihydroxylalcanes et les dicarboxylalcanes.

6. Structure a nanoparticules selon l'une des revendications 1 a 5, caracterisee en ce que la structure a nanoparticules (3) est integree avec une structure de transistor pour former un element de commande pour le courant entre les bornes du transistor.

7. Structure a nanoparticules selon la revendication 6, caracterisee en ce qu'une structure tunnel resonante est formee par une ou plusieurs couches de nanoparticules (13, 15) incluses entre des barrieres isolantes et en ce que cette structure tunnel est...

...elle en reponse a une tension appliquee a la structure tunnel resonante.

8. Structure a nanoparticules selon l'une des revendications 1 a 7, caracterisee en ce que les ligands (13)...

...ou pour empecher ou entraver l'adsorption de substances differentes dudit analyte.

9. Structure a nanoparticules selon l'une des revendications 1 a 8, caracterisee en ce que la surface d'au moins certaines nanoparticules (11) est modifiee pour favoriser l'adsorption d'un analyte specifique et/ou pour entraver ou empecher l'adsorption de substances differentes dudit analyte.

10. Utilisation d'une structure a nanoparticules selon l'une des revendications 1 a 9 comme capteur pour detecter selectivement un ou ...

...detecter un ou plusieurs analytes dans une phase liquide ou gazeuse comprenant une structure a nanoparticules (3) selon la revendication 1 et comprenant en outre un substrat (1) et des moyens

- pour detecter la conductivite de ladite structure a **nanoparticules** (3).
12. Capteur selon la revendication 11, caracterise en ce que les ligands (13, 15...
- ...la revendication 11 ou 12, caracterise en ce que la surface d'au moins certaines **nanoparticules** (11) est modifiee pour favoriser l'adsorption d'un analyte specifique et/ou entraver ou...
- ...l'une des revendications 11 a 13, caracterise en ce qu'il est concu pour **detecter** une ou plusieurs des substances suivantes : **ammoniac** , ethanol, propanol, toluene, eau, hexanes.
15. Capteur selon l'une des revendications 11 a 14...
- ...qu'il comprend un element amplificateur commande par le courant circulant dans la structure a **nanoparticules** (3).
16. Capteur selon la revendication 15, caracterise en ce que la structure a **nanoparticules** est agencee de telle maniere qu'elle commande le courant de base d'un transistor...
- ...selon l'une des revendications 15 ou 16, caracterise en ce que la structure a **nanoparticules** (3) est incluse entre deux barrieres tunnel et forme un dispositif tunnel resonant.
18. Capteur selon l'une des revendications 15 a 17, caracterise en ce que la structure a **nanoparticules** (3) est integree avec ledit element amplificateur dans un circuit integre (CI).
19. Capteur selon...
- ...en ce qu'une membrane chimiquement selective est disposee sur ou dans la structure a **nanoparticules** .
20. Procede pour produire une structure a **nanoparticules** selon la revendication 1 destinee a etre utilisee dans un dispositif electronique et/ou un...
- ...des revendications 11 a 19, comprenant les etapes :
- a) liaison d'une premiere couche de **nanoparticules** (11) a un substrat (1) par des molecules de ligands (13) ;
 - b) liaison de molecules de ligands bifonctionnels ou polyfonctionnels (15) a ladite premiere couche de **nanoparticules** (11), la taille des molecules de ligands (15) etant ajustee de telle sorte qu'il se forme entre lesdites **nanoparticules** (11) des cavites ayant une taille permettant a l'analyte a detecter de diffuser dans lesdites cavites ; et
 - c) liaison d'une couche supplementaire de **nanoparticules** (11) auxdits ligands bifonctionnels ou polyfonctionnels (15).
21. Procede selon la revendication 20, caracterise en...
- ...que les etapes b) et c) sont repetees pour creer une pluralite de monocouches de **nanoparticules** empilees sur ledit substrat (1).
22. Procede selon la revendication 20 ou 21, caracterise en ce qu'il comprend l'etape de modification de la surface d'au moins certaines **nanoparticules** (11) pour favoriser l'adsorption d'un analyte specifique et/ou pour entraver ou empecher...

Detecting target analyte/biomarker, involves mixing nanostructure-based assembly with biological fluid sample and analyzing mixture of nanostructure-based assembly and biological fluid sample with sensor technology - nanostructure-based assembly for biosensor or DNA biosensor manufacture and target analyte or biomarker detection

AUTHOR: MELKER R J; HAYES R L; WANG K K; DENNIS D M

PATENT ASSIGNEE: UNIV FLORIDA RES FOUND INC 2005

PATENT NUMBER: WO 200533707 PATENT DATE: 20050414 WPI ACCESSION NO.: 2005-296174 (200530)

PRIORITY APPLIC. NO.: US 678506 APPLIC. DATE: 20031002

NATIONAL APPLIC. NO.: WO 2004US29131 APPLIC. DATE: 20040903

LANGUAGE: English

...ABSTRACT: and protease-specific spectrin breakdown products. The target analyte/biomarker is chosen from acetaldehyde, acetone, ammonia, CO, chloroform, dichlorobenzene, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, O-toluidine, pentane sulfides and sulfides, hydrogen sulfide, 2-(n-morpholine)ethanesulfonic acid (MES) and Me₂S. The sensor technology is chosen from surface-acoustic-wave sensors, fluid sensor technology, semiconductive gas sensors, mass...

... of the surrogate marker from the amplitude. The nanostructure-based assembly comprises at least one nanoparticle comprising a surrogate marker and an unit for detecting a target analyte/biomarkers, where the unit for detecting the target analyte/biomarker is bound to the nanoparticle in such a way as to affect the release of the surrogate marker when in...

4/3,KWIC/5 (Item 2 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0364038 DBR Accession No.: 2005-09742 PATENT

Diagnosing and treating a condition, e.g. anemia, comprises administering a nanoparticle -based assembly having a nanoparticle, surrogate marker, mode for detecting a specific chemical entity, and a payload, to a patient - for atherosclerosis, glycogen storage disease, leukemia, anaplastic lymphoma, hemophilia, thrombocytopenia, anemia diagnosis, therapy and gene therapy

AUTHOR: MELKER R J; DENNIS D M

PATENT ASSIGNEE: MELKER R J; DENNIS D M 2005

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NATIONAL APPLIC. NO.: US 744789 APPLIC. DATE: 20031223

LANGUAGE: English

Diagnosing and treating a condition, e.g. anemia, comprises administering a nanoparticle -based assembly having a nanoparticle, surrogate marker, mode for detecting a specific chemical entity, and a payload, to a patient...

...ABSTRACT: and treating (M1) a condition, disease, or disorder comprises: (a) administering a composition comprising a nanoparticle -based assembly, which has a nanoparticle, surrogate marker, and a mode for detecting a specific chemical entity (SCE), and a payload...

... disease, or disorder, comprises: (a) administering to a patient, a composition comprising at least one nanoparticle -based assembly, which has a nanoparticle, surrogate marker, and a mode for detecting a specific chemical entity (SCE), and a payload...

...disease/disorder states of a patient, is also disclosed. BIOTECHNOLOGY - Preferred Method: In (M1), the **nanoparticle** is a nanotube. The SCE-detecting mode is chosen from an antibody, protein and aptamer...

... or mixture containing homogenized solid materials chosen from feces, tissues, and biopsy samples. The SCE- **detecting** mode has a specific action on compounds chosen from acetaldehyde, acetone, **ammonia** , carbon monoxide, chloroform, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, O-toluidine, pentane sulfides and sulfides, hydrogen...

... monocytic markers, maturity status markers, alpha-fetoprotein, beta2-microglobulin, and beta human chorionic gonadotropin. The **nanoparticle** is formed with an interior void that contains the surrogate marker, where the **nanoparticle** has at least one open end to provide access to the interior void. The interior void also contains a payload. The **nanoparticles** further include an end-cap to block the open end. The end-cap is a...

... a maximum dimension of less than 100 microm. The end-cap is attached to the **nanoparticle** by covalent bonds. The **nanoparticle** is in the form of a tubular body, and SCE-detecting mode is attached to the end-cap. The **nanoparticle** is composed of silica or polymer. The SCE-detecting mode is attached to a surface of the **nanoparticle** using copolymerization. The SCE-detecting mode is incorporated into the **nanoparticle** . The **nanoparticle** is produced in a shape chosen from spherical, elliptical, cubic, cylindrical, tetrahedron, polyhedral, irregular-prismatic, icosahedral and cubo-octahedral. The **nanoparticle** has a dimension of less than 500 nm. The surface of the **nanoparticle** is stealthy. The payload is chosen from genetic materials, RNA, oligonucleotides, polynucleotides, peptides, proteins, enzymes...

DESCRIPTORS: **nanoparticle** -based assembly, surrogate marker, appl., atherosclerosis, glycogen storage disease, leukemia, anaplastic lymphoma, hemophilia, thrombocytopenia, anemia...

4/3,KWIC/6 (Item 1 from file: 73)
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Sensor activity of thin polymer films containing lead nanoparticles
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Sensor activity of thin polymer films containing lead nanoparticles

Thin poly(p-xylylene) films containing lead **nanoparticles** were prepared by vacuum deposition technique. The vapors of p-xylylene monomer and lead

were...

...obtained were characterized by electric conductivity measurements during film samples formation. Such metallopolymer films exhibit **sensor** activity in the presence of **ammonia** in the atmospheric air. The influence of air humidity and the co-operative effect of **ammonia** together with water vapors on film resistance were studied. (c) 2002 Elsevier Science B.V...

MEDICAL DESCRIPTORS:

sensor; film; **nanoparticle** ; vacuum; technique; polymerization; electric conductivity; air; humidity; water vapor; room temperature; conference paper; priority journal

4/3,KWIC/7 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
(c) 2006 ProQuest Info&Learning. All rts. reserv.

02073891 ORDER NO: AADAA-IC820705

Studies on lean nitrogen oxide reduction with ammonia : Catalysts and sensors

Author: Wallin, Mikaela

Degree: Ph.D.

Year: 2005

Corporate Source/Institution: Chalmers Tekniska Hogskola (Sweden) (0419)

Source: VOLUME 66/03-C OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 696. 66 PAGES

ISBN: 91-7291-554-4

Publisher: Chalmers University of Technology, SE-412 96 Goteborg, Sweden

Studies on lean nitrogen oxide reduction with ammonia : Catalysts and sensors

...increased, as NO oxidation sites became available. It was further shown that transient supply of **ammonia** enhanced the total NO reduction up to five times compared to continuous supply.

The sensing layer of an **ammonia sensor** was investigated by studying a model system consisting of Pt **nanoparticles** supported on silica. In situ FTIR spectroscopy provided evidence for NH_2 species...

4/3,KWIC/8 (Item 2 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
(c) 2006 ProQuest Info&Learning. All rts. reserv.

01918223 ORDER NO: AADAA-I3070663

Enzymes in thermostable biosensors and nanomaterials

Author: Li, Ju

Degree: Ph.D.

Year: 2002

Corporate Source/Institution: University of Kentucky (0102)

Source: VOLUME 63/11-B OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 5208. 167 PAGES

ISBN: 0-493-90619-3

...It has the advantage of tolerating temperatures as high as 135°C, compared to **ammonia gas sensors** which can tolerate no more than 60°C.

As Nanotechnology is becoming increasingly integrated...

...has become a way to fabricate nanoscale systems with new or improved biological properties. Alumina **nanoparticles** can be functionalized with biological molecules through condensation of surface hydroxyls between alumina with phosphoryl...

...The enzyme pepsin has one phosphoryl group on its serine 68 residue. The alumina-pepsin **nanoparticles** are compared with the corresponding coupling with micro-sized particles. The capacity of the **nanoparticles** to binding pepsin on **nanoparticles** was about ten times larger than that on micro-sized particles. Both commercial γ -alumina **nanoparticles** and amorphous alumina **nanoparticles** derived from tetrametallic molecular precursors were used for the conjugation studies. Also, a recombinant glutathione...

...transferase (GST) was phosphorylated by a protein kinase. The conjugation of phosphorylated GST with alumina **nanoparticles** was compared with the coupling of native GST with **nanoparticles**. The coupling process is highly reversible, with over 93% bound enzyme being released after incubation with phosphate solution. Alumina **nanoparticles** can be assembled together with the dimeric recombinant phosphorylated GST to form higher order structures.

4/3,KWIC/9 (Item 1 from file: 16)
DIALOG(R) File 16:Gale Group PROMT(R)
(c) 2006 The Gale Group. All rts. reserv.

12334422 Supplier Number: 132129909 (USE FORMAT 7 FOR FULLTEXT)
Applied Nanotech, Inc. and MITSUI & CO. LTD. Announce a Memorandum Of Understanding.
PR Newswire, pNA
Jan 28, 2003
Language: English Record Type: Fulltext
Document Type: Newswire; Trade
Word Count: 614

... products will include new CNT (carbon nanotube) electron sources in both diode and triode mode, **nanoparticle sensors** (hydrogen, humidity and ammonia), miniature x-ray tubes using CNT cathodes, and new nanomaterials (silicon quantum dots, magnetic CNTs...

...nanowires, carbon nanotube composites, magnetic carbon nanotubes, etc., use of new nano-sized materials and **nanoparticles** in **sensor** applications for hydrogen, humidity, ammonia, and others, nano-electronic devices such as vacuum nano-transistors, ultra-capacitors, microwave matrix sources...

4/3,KWIC/10 (Item 2 from file: 16)
DIALOG(R) File 16:Gale Group PROMT(R)
(c) 2006 The Gale Group. All rts. reserv.

11575675 Supplier Number: 122921514 (USE FORMAT 7 FOR FULLTEXT)
New sensors, automated analyzers spur clinical diagnostics advances. (Part 2 of 2 parts)
Simonsen, Michael
The BBI Newsletter, v27, n10, p253(6)
Oct, 2004
Language: English Record Type: Fulltext
Document Type: Newsletter; Trade

Word Count: 3920

... for commercialization

partners for
diagnostics.

Mesa Institute for
Nanotechnology
(Twente, the
Netherlands)

Nanotechnology-based
vibrational sensors for
analysis of ammonia in
breath, lithium detec-
tion in whole blood.
Silicon microneedles for
painless blood micro...

Research-use proto-
types developed.

...develop-

(Nanjing, China)

field-effect transistor
(ENFET) employing MnO₂
nanoparticles for
enhanced sensitivity

ment for in-vitro
glucose testing.

Oxford Biosensors
(Oxfordshire, UK)

Carbon ink-based elec-
trochemical sensor...

Prototype handheld

4/3,KWIC/11 (Item 1 from file: 94)

DIALOG(R)File 94:JICST-EPlus

(c)2006 Japan Science and Tech Corp(JST). All rts. reserv.

05995389 JICST ACCESSION NUMBER: 05A0204883 FILE SEGMENT: JICST-E

Construction of PEGylated Gold Colloid-Assembled Surface for High
Performance Biosensor

ISHII TAKEHIKO (1); SUZUKI YUKO (1); AKIYAMA YOSHITSUGU (2); KATAOKA
KAZUNORI (2); OTSUKA HIDENORI (3); NAGASAKI YUKIO (4)

(1) Sci. Univ. Tokyo, Graduate School of Industrial Sci. and Technol., JPN
; (2) Univ. Tokyo, Graduate School of Engineering, JPN; (3) National Inst.
Materials Sci., JPN; (4) Univ. of Tsukuba

Kobunshi Ronbunshu(Japanese Journal of Polymer Science and Technology),
2005, VOL.62,NO.2, PAGE.81-86, FIG.6, REF.23

JOURNAL NUMBER: G0122ABI ISSN NO: 0386-2186 CODEN: KBRBA

UNIVERSAL DECIMAL CLASSIFICATION: 544.23:542.9+ 576/577.087

LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal

ARTICLE TYPE: Original paper

MEDIA TYPE: Printed Publication

...ABSTRACT: then it was treated by a primary amino group via a reductive
amination reaction with ammonia. The obtained amino-PEGylated gold
colloids showed high dispersion stability under the physiological
conditions. The amino-PEGylated gold colloid was fixed on the surface
plasmon sensor surface via covalent linkage using a NHS-linker. The
amine-PEG-gold colloid surface prevented...

IDENTIFIERS: nanoparticle

4/3,KWIC/12 (Item 2 from file: 94)

DIALOG(R)File 94:JICST-EPlus

(c)2006 Japan Science and Tech Corp(JST). All rts. reserv.

05681266 JICST ACCESSION NUMBER: 04A0020624 FILE SEGMENT: JICST-E

Composite Nanofiber Interface for Chemical and Biochemical Sensor

DING B (1); KIM J (1); SHIRATORI S (1)

(1) Keio Univ.

Denki Gakkai Kemikaru Sensa Kenkyukai Shiryo(Papers of Technical Meeting on
Chemical Sensor, IEE Japan), 2003, VOL.CHS-03,NO.56-86, PAGE.113-116,
FIG.8, REF.11

JOURNAL NUMBER: L2895BAU

UNIVERSAL DECIMAL CLASSIFICATION: 543.084 543.9:577.1

LANGUAGE: English COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Conference Proceeding

ARTICLE TYPE: Original paper

MEDIA TYPE: Printed Publication

...ABSTRACT: electrospinning of homogenous solution of poly(vinyl
alcohol)(PVA), poly(acrylic acid)(PAA) and TiO₂ nanoparticles . A
series of nanofiber samples with different concentration of PAA were
fabricated on the QCM...

...resonance frequency shift due to additional mass loading. The results
showed the sensing properties for ammonia gas were strongly affected
by the concentration of PAA in nanofibers. And the sensor was
suitable to detect the low concentration of ammonia gas. (author
abst.)

4/3,KWIC/13 (Item 3 from file: 94)

DIALOG(R)File 94:JICST-EPlus

(c)2006 Japan Science and Tech Corp(JST). All rts. reserv.

05583241 JICST ACCESSION NUMBER: 03A0687135 FILE SEGMENT: JICST-E

Quartz crystal ammonia gas sensor using a layer-by-layer self assembly
thin film

KIM J H (1); SHIRATORI S (1)

(1) Keio Univ., Yokohama, Jpn

Denshi Joho Tsushin Gakkai Gijutsu Kenkyu Hokoku(IEIC Technical Report
(Institute of Electronics, Information and Communication Engineers),
2003, VOL.103,NO.279(OME2003 45-57), PAGE.63-68, FIG.11, REF.21

JOURNAL NUMBER: S0532BBG ISSN NO: 0913-5685

UNIVERSAL DECIMAL CLASSIFICATION: 621.382+ 543.084

LANGUAGE: English COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal

ARTICLE TYPE: Original paper

MEDIA TYPE: Printed Publication

Quartz crystal ammonia gas sensor using a layer-by-layer self assembly
thin film

ABSTRACT: Nanoporous and hetero structure thin film consisted of weak
polyelectrolytes and TiO₂ nanoparticles was fabricated by immersing
the thin film assembled via layer-by-layer self assembly (LBL...
...poly(acrylic acid) were broken in acidic water, which contributed to
separate the agglomerated TiO₂ nanoparticles deposited on the surface
of thin film. In order to evaluate the gas sensitivity of...

4/3,KWIC/14 (Item 1 from file: 144)

DIALOG(R)File 144:Pascal

(c) 2006 INIST/CNRS. All rts. reserv.

17009833 PASCAL No.: 05-0071586

Development of functionalized terbium fluorescent nanoparticles for
antibody labeling and time-resolved fluoroimmunoassay application

ZHIQIANG YE; MINGQIAN TAN; GUILAN WANG; JINGLI YUAN

Department of Analytical Chemistry, Dalian Institute of Chemical Physics,
Chinese Academy of Sciences, Dalian 116012, China
Journal: Talanta : (Oxford), 2005, 65 (1) 206-210
Language: English

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Development of functionalized terbium fluorescent nanoparticles for antibody labeling and time-resolved fluoroimmunoassay application

Silica-based functionalized terbium fluorescent nanoparticles were prepared, characterized and developed as a fluorescence probe for antibody labeling and time-resolved fluoroimmunoassay. The nanoparticles were prepared in a water-in-oil (W/O) microemulsion containing a strongly fluorescent Tb...

... with ammonia water. The characterizations by transmission electron microscopy and fluorometric methods show that the nanoparticles are spherical and uniform in size, 45 +/- 3 nm in diameter, strongly fluorescent with fluorescence...

... a long fluorescence lifetime of 2.0 ms. The amino groups directly introduced to the nanoparticle's surface by using AEPS in the preparation made the surface modification and bioconjugation of the nanoparticles easier. The nanoparticle-labeled anti-human alpha-fetoprotein antibody was prepared and used for time-resolved fluoroimmunoassay of...

English Descriptors: Nanoparticle ; Time resolution; Fluorescence spectrometry; Microemulsion; Ammonia ; Transmission electron microscopy; Quantum yield; Lifetime; Chemical modification; Human; Chemical analysis; Detection limit; Variation coefficient; Terbium; Antibody; Silica; Water; Acetate; Octanol; Cyclohexane; Immunological method; Fetoprotein-ANA; Serum...

French Descriptors: Nanoparticule ; Resolution temporelle; Spectrometrie fluorescence; Microemulsion; Ammoniac ; Microscopie electronique transmission; Rendement quantique; Duree vie; Modification chimique; Homme; Analyse chimique; Limite detection ; Coefficient variation; Terbium; Anticorps; Silice; Eau; Acetate; Octanol; Cyclohexane; Methode immunologique; Foetoproteine-ANA; Serum-SUB...

Spanish Descriptors: Nanoparticula ; Resolucion temporal; Espectrometria fluorescencia; Microemulsion; Amoniaco; Microscopia electronica transmission; Rendimiento quantico; Tiempo vida; Modificacion quimica...

4/3,KWIC/15 (Item 2 from file: 144)
DIALOG(R) File 144:Pascal
(c) 2006 INIST/CNRS. All rts. reserv.

16477103 PASCAL No.: 04-0120978
Chemiresistor coatings from Pt- and Au- nanoparticle /nonanedithiol films: Sensitivity to gases and solvent vapors
JOSEPH Y; GUSE B; YASUDA A; VOSSMEYER T
Materials Science Laboratories Sony International (Europe) GmbH, D-70327 Stuttgart, Germany
Journal: Sensors and Actuators, B: Chemical, 2004, 98 (2-3) 188-195
Language: English

Chemiresistor coatings from Pt- and Au- nanoparticle /nonanedithiol films: Sensitivity to gases and solvent vapors

... by-layer self-assembly using 1,9-nonanedithiol (NT) and dodecylamine-stabilized Pt- or Au- nanoparticles . The film thickness, as determined by atomic force microscopy (AFM), is 66 +- 2 and 31...

... interpreted with the assumption that NH₃ and CO bind to vacant sites on the metal nanoparticle cores, whereas water and toluene interact preferably with the NT linker molecules. (c) 2003 Elsevier...

English Descriptors: Nanoparticles ; Chemiresistors; Vapor; Theory; Platinum; Gold plating; Ammonia ; Carbon monoxide; Nanostructured materials; Toluene; Polytetrafluoroethylenes; Isotherms; Absorption; Signal to noise ratio; Film preparation; Deposition; Chemical sensors ; Experiments

4/3,KWIC/16 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2006 INIST/CNRS. All rts. reserv.

14867381 PASCAL No.: 01-0014008
Gas sensitivity of composite Langmuir-Blodgett films of Fe₂O₃ nanoparticle -copper phthalocyanine
HUO L H; LI X L; LI W; XI S Q
Chinese Acad of Sciences, Changchun, China
Journal: Sensors and Actuators, B: Chemical, 2000, 71 (1-2) 77-81
Language: English

Gas sensitivity of composite Langmuir-Blodgett films of Fe₂O₃ nanoparticle -copper phthalocyanine
The Langmuir-Blodgett (LB) composite films, ferric oxide nanoparticle composite with tris-(2,4-di-t-amylphenoxy)-(8-quinolinolyl) copper phthalocyanine (CuPcA2), were obtained...

... of the composite films and the pure ferric oxide and pure CuPcA2 LB films to ammonia and ethanol were measured at room temperature. The composite films could be used as the C₂H₅OH sensors in the range of 2-8 or 100-200 ppm. The XPS data suggested that the adduct complex NH₃-CuPcA2 was formed after the capped film was exposed to the detected gas of ammonia .

English Descriptors: Nanoparticle -copper phthalocyanine; Theory; Langmuir Blodgett films; Iron oxides; X ray photoelectron spectroscopy; Sensitivity analysis; Ammonia ; Ethanol; Composite materials; Nanostructured materials; Chemical sensors ; Experiments

4/3,KWIC/17 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2006 INIST/CNRS. All rts. reserv.

12976812 PASCAL No.: 97-0254619
Preliminary study of the interaction of metal nanoparticle -containing poly-p-xylylene films with ammonia
SERGEEV G; ZAGORSKY V; PETRUKHINA M; ZAV'YALOV S; GRIGOR'EV E; TRAKHTENHERG L
Department of Chemistry, Moscow State University, 119899 Moscow, Russia; State Scientific Center of RF Karpov Institute of Physical Chemistry, Moscow, Russia
Journal: Analytical communications, 1997, 34 (4) 113-114
Language: English

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Preliminary study of the interaction of metal nanoparticle -containing poly-p-xylylene films with ammonia

English Descriptors: Xylene polymer; Encapsulation; Metal particle; Nanometer scale; Lead; Electrical conductivity; Electric resistivity; Gas detector ; Ammonia -ANA

French Descriptors: Xylene polymere; Encapsulation; Particule metallique; Echelle nanometrique; Plomb; Conductivite electrique; Resistivite electrique; Detecteur de gaz; Ammoniac -ANA

4/3,KWIC/18 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01340017

NANOTUBE SENSOR DEVICES FOR DNA DETECTION

DISPOSITIFS DE DETECTION A NANOTUBES, DESTINES A LA DETECTION DE SEQUENCES D'ADN

Patent Applicant/Assignee:

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200624023 A2 20060302 (WO 0624023)

Application: WO 2005US30487 20050824 (PCT/WO US2005030487)

Priority Application: US 2004604293 20040824; US 2004629604 20041119

Designated States:

(All protection types applied unless otherwise stated - for applications 2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL
PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU
ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU LV MC NL
PL PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 14643

Fulltext Availability:

Detailed Description

Detailed Description

... using SWNTs grown by chemical vapor deposition (CVD) at 900'C using
21
dispersed iron nanoparticles as growth promoter and a methane/hydrogen
gas mixture. Electrical leads were patterned on top...other reaction with
a chemical or biochemical substrate thereby influencing sensor 10 to
provide a detectable response. For example, amplifier group 46 may
comprise urease.

Step (d) above may comprise treating with a urea solution, to produce
ammonia and carbon dioxide if bound probe 46 is present, so as to modify
the pH of the solution and thereby detectably change the signal of
sensor 10. Other examples of enzyme systems which may be employed are
cholinesterase; peroxidase (e.g.

HRP); glucose oxidase, and the like. Other examples of amplifier group 46
are ferrocene, metal nanoparticles, labels (nanoparticles, proteins,
etc.), and the like.

[001591 FIG. 9E shows schematically an alternative exemplary assay
embodiment...

...DNA from genomic DNA in the vicinity of the nanotube device 10. For
example, labels (nanoparticles, proteins, etc.) may be used for
separation of the target DNA from genomic DNA as...

4/3,KWIC/19 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2006 WIPO/Univentio. All rts. reserv.

01290916 **Image available**

SYSTEM AND METHOD FOR REAL-TIME DIAGNOSIS, TREATMENT, AND THERAPEUTIC DRUG
MONITORING

SYSTEME ET PROCEDE DE DIAGNOSTIC, DE TRAITEMENT ET DE PHARMACOVIGILANCE
THERAPEUTIQUE EN TEMPS REEL

Patent Applicant/Assignee:

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designated states except: US)

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GOLD Mark S, 5745 S.W. 75th St. #324, Gainesville, FL 32608, US, US
(Residence), US (Nationality), (Designated only for: US)

DENNIS Donn Michael, 4949 SW 95th Terrace, Gainesville, FL 32608-4189, US
, US (Residence), US (Nationality), (Designated only for: US)

Legal Representative:

EFRON Margaret (et al) (agent), Saliwanchik, Lloyd & Saliwanchik, P.O.
Box 142950, Gainesville, FL 32614-2950, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200598429 A2 20051020 (WO 0598429)

Application: WO 2005US6355 20050228 (PCT/WO US05006355)

Priority Application: US 2004788501 20040226

Parent Application/Grant:

Related by Continuation to: US 2000708789 20001108 (CON); US 2004788501
20040226 (CIP); US 2002178877 20020624 (CIP); US 200254619 20020122
(CIP); US 2003744789 20031223 (CIP); US 2003345532 20030116 (CIP); US
2002274829 20021021 (CIP); US 2002154201 20020522 (CIP); US 2003722620
20031126 (CIP)

Designated States:

(All protection types applied unless otherwise stated - for applications 2004+)

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US (patent) UZ VC VN
YU ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU MC NL PL
PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 25632

Fulltext Availability:

Detailed Description

Claims

English Abstract

...or treating diseases as well as monitoring disease treatment. For diagnosis, the present invention uses **nanoparticle** -based assemblies, which comprise a **nanoparticle** ; a surrogate marker; and a means for detecting a specific chemical entity. In certain embodiments, **nanoparticle** -based assemblies include a payload for simultaneous diagnosis and treatment of disease. In further embodiments...

French Abstract

...du traitement des maladies. Dans le domaine du diagnostic, l'invention fait intervenir des ensembles **nanoparticulaires** qui contiennent une **nanoparticule** ; un marqueur de substitution; ainsi que des moyens de detection d'une entite chimique specifique. Dans certains modes de realisation, les ensembles **nanoparticulaires** contiennent une charge qui permet de diagnostiquer et de traiter simultanement une maladie. Dans d ...

Detailed Description

... and the identification of biomarkers for specific diseases and/or therapeutic drugs. Nanotechnology, such as **nanoparticles** , offers many advantages when used for applications such as the delivery of bioactive agents (i...

...gene therapy, immunosuppressants, chemotherapeutics), and drug uptake and degradation (i.e., enzyme encapsulation).

For example, **nanoparticles** have been proposed as providing site-specific distribution of drugs to a target site. Appropriately...

...In a preferred embodiment, the nanostructure-based assembly of the invention is composed of a **nanoparticle** that contains the following components: (a) a means for detecting an SCE; and (b) a surrogate marker. For simultaneous diagnosis and treatment of disease, the **nanoparticle** preferably contains an additional component, (c) a "payload," for treating the disease that is associated...

...the SCE. Any combination of these components can be attached to any surface of the **nanoparticle** .

Further embodiments of the invention enable real-time monitoring of disease treatment. Therapeutic drug concentration...

...SCE-detector and a target SCE induces the release of the surrogate marker from the nanoparticle. Advantageously, the concentration of the released surrogate marker can be correlated to the amount of...

...treatment is delivered with disease diagnosis. With these embodiments, the nanostructure-based assembly comprises a nanoparticle, a means for detecting an SCE, a surrogate marker, and a payload. In operation, these ...is an accurate indicator of the concentration of therapeutic drug in the blood stream.

Nanoparticles

Nanostructure-based assemblies offer timely, and effective detection, notification, and treatment of a disease of interest. Such assemblies are based on 5 nanoparticles, which provide a mechanism for the targeted delivery and release of detectable markers and/or bioactive treatment agents to selected sites within the body.

According to the present invention, nanoparticles can be produced in a wide range of sizes and shapes, and composed...

...are of a maximum dimension less than 100-150 nm. The "maximum dimension" of a nanoparticles is the maximum distance between any two points in the nanoparticle. In a preferred embodiment, the nanoparticles are in the form of tubular bodies (also known as "nanotubes"), which are either hollow...

...open ends or one or both closed ends.

In accordance with the present invention, the nanoparticle-based assemblies are composed of biodegradable substances. In other embodiments, the nanoparticle-based assemblies of the invention are composed of biocompatible substances.

Methods of preparation of nanoparticles are well known in the art. For example, the preparation of monodisperse sol-gel silica...

...al., "Synthesis of Microporous Silica Spheres," J. Colloids and Interface Science, 227, 302 (2000).

Nanoparticles, in accordance with the present invention, can be prepared from a single material or a...

...of materials including, but not limited to, polymers, semiconductors, carbons, or Li⁺ intercalation materials. Metal nanoparticles include those made from gold or silver. Semiconductor nanoparticles include those made from silicon or germanium. Polymer nanoparticles include those made from biocompatible or biodegradable polymers. The ability to make nanoparticles from a wide variety of materials or combination of materials allows the creation of nanoparticles with desired biochemical properties such as biocompatibility, including immunogenic compatibility, and/or, biodegradability. In comparison, certain biological delivery systems, such as viral vectors, can cause significant immunogenic phenomena.

Nanoparticles of the present invention can be synthesized using a template synthesis method. For example, nanoparticles can be synthesized using templates prepared from glass (Tonucci, R.J. et al.,

Science 258...

...and a variety of other materials (Ozin, G.A., Adv. Mater., 4, 612 1992)). Alternatively, **nanoparticles** can be prepared using a self-assembly process, as described in Wang, Z.L., "Structural...

...13-30 (1998).

In one embodiment, a nanostructure-based assembly of the invention contains a **nanoparticle**, which has one or more surfaces functionalized to allow attachment of SCE-detectors to the surface. Such "functionalized" **nanoparticles** have at least one surface modified to allow for directed (also referred to as "vectoring...

...or controlled release of the surrogate marker (and payload, when available). In certain embodiments, the **nanoparticle** is formed with an interior void. Different chemical and/or biochemical functional groups can be applied to the inside and/or outside surfaces of the **nanoparticle** to enable the attachment of an SCE-detector, surrogate marker, and/or payload on a **nanoparticle** surface.

In another embodiment, the nanostructure-based assembly contains a **nanoparticle** formed with an interior void to contain a surrogate marker, a payload, and a detachable...

...presence of a target SCE, the SCE-detector mechanically detaches the end-cap from the **nanoparticle** to release the surrogate marker for analysis by sensor technology.

Simultaneously, the payload is released for the treatment of a disease.

In a preferred embodiment, the **nanoparticle** is in the form of a nanotube that is hollow and has a first open...

...the end-cap, the surrogate marker and payload are released with the uncapping of the **nanoparticle**.

The uncapping mechanism may require the use of energy-bearing biomolecular motors such as, but...

...filament elongation model for actin-based motors," Biopolymers J, 82:605-617 (2002)). Once the **nanoparticle** is uncapped, the released surrogate marker can then be detected using sensor technology known in...

...activity and decreased use of dosage amounts.

Nanotubes

A number of patents and publications describe **nanoparticles** in the form of tubes (nanotubes). For example, U.S. Patent No. 5,482,601...

...substrate aluminum surface (Hornyak, G.L., et al., "Fabrication, Characterization and Optical Properties of Gold- **Nanoparticle** /Porous-Alumina Composites: The Non-Scattering Maxwell Garnett Limit," J Phys. Chem. B., 10 1: 1548...

...the other end.

Suitable end-caps used to block a nanotube opening include, for example, **nanoparticles** having a diameter slightly larger than the inside diameter of the **nanoparticle** so as to occlude the open end of the

nanoparticle . End-caps are any piece of matter and can be composed of materials that are chemically or physically similar (or dissimilar) to the **nanoparticle** . The end-cap can be a particle that has a maximum dimension of less than...

...3-Si-(CH₂)₃-SH could be attached to a silica nanotube and a gold **nanoparticle** attached as the end-cap using the -SH end of this molecule. It is well...
...form spontaneous As-S bonds with gold surfaces.

Contemplated end-caps for the invention include **nanoparticles** that can be electrophoretically placed within the mouths of nanotubes so that the entire mouth of the nanotube is blocked when disulfide bonds are formed between the nanotube and the **nanoparticle** as described in Miller, S.A. and C.R. Martin, "Electroosmotic Flow in Carbon Nanotube..."

...endcaps can be suspended in solution together with the activated disulfide labeled nanotubes. Here, the **nanoparticle** caps can spontaneously self-assemble to the nanotubes. The self-assembly of gold nanospheres and...

...1202-1205 (1999)), and antigen/antibody interactions (Shenton, W. et al., "Directed Self-Assembly of **Nanoparticles** into Macroscopic Materials Using Antibody-Antigen Recognition," Adv. Mater., 11:449 (1999)).

Preferred nanotubes...

...e., surrogate marker and/or payload material). Methods for attaching an end-cap to a **nanoparticle** include, but are not limited to, using electrostatic attraction, hydrogen bonding, acid and/or basic sites located on the endcap/ **nanoparticle** , covalent bonds, and other chemical linkages.

In a preferred embodiment, the detecting means is attached...

...affect the release of the surrogate marker and/or payload material via uncapping of the **nanoparticle** . For example, the uncapping mechanism is based upon the detection by the detecting means of...

...ultraviolet (UV), or visible absorbance or fluorescence, or mass spectrometers.

I 0 Functionalization of the **Nanoparticles**

According to the present invention, **nanoparticles** can be prepared having different chemically or biochemically functionalized surfaces to enable attachment of an SCE-detecting means, surrogate marker, and/or payload. Methods used to functionalize a **nanoparticle** surface depend on the composition of the **nanoparticle** 5 and are well known in the art. For example, functionalization of silica **nanoparticles** is accomplished using silane chemistry. With silane chemistry, different functional groups can be attached to the surfaces of the **nanoparticle** by attaching a functional group to the **nanoparticle** surface while the **nanoparticles** are embedded within the pores of the template. Then, a hydrolytically unstable silane is reacted with the surface silanol sites on the **nanoparticle** to obtain covalent oxygen/silicon bonds between the surface and the silane. Additional functional groups can also be attached to the **nanoparticle** surface after dissolution of the template.

The surface of polymer **nanoparticles** can also be functionalized using well known chemical methods. For example, methods employed for polylactide...

...groups to enable attachment of a detecting means, surrogate marker, and/or payload to a **nanoparticle** surface.

Alternatively, functional groups can be introduced by copolymerization.

Natural amino acids are sterically similar...

...standard methods and used for random copolymerization with lactide. In accordance with the present invention, **nanoparticles** can have functional groups on any surface to enable the attachment of an SCE-detecting...

...addition, the detecting means, surrogate marker, and/or payload can be incorporated into the **nanoparticle** framework, which can include chitosan, PEGylated PLGA (poly(lactic-co)-glycolic acid), or other PEGylated...

...maleimide can be incorporated into chain-terminated thiols on the outer surface of the **nanoparticles**. Alternatively, marker, and/or payload can be incorporated into **nanoparticle** frameworks composed of biodegradable and/or resorbable materials including, for example, polylactide based polymers as described above.

For **nanoparticles** comprising a hollow void in which the surrogate marker can be contained, a surrogate marker...

...Flow in Carbon Nanotube Membranes," J. Am. Chem. Soc., 123(49):12335-12342 (2001). Alternatively, **nanoparticles** embedded within the synthesis membrane can be filled with a surrogate marker by vacuum filtering a...

...the synthesis membrane. (See Parthasarathy, R. and C.R. Martin, Nature, 369:298 (1994)). For **nanoparticles** prepared by formation within an alumina template film prior to removal of the alumina from...

...needed.

In one embodiment, a detecting means is attached to the outer surface of the **nanoparticle** via any of the aforementioned functional groups. The controlled release of the surrogate marker and...

...payload are accomplished by the release of the end-cap, which is attached to the **nanoparticle** via chemically labile bonds.

Yet another embodiment provides a **nanoparticle** that has the detecting means, the surrogate marker, and the payload (when present) applied to the outside, exposed surface of the **nanoparticle** - All of these components are attached to the surface of the **nanoparticle** via chemically labile bonds, which allow for the release of these components under specific conditions...

...to proteins. Such aptamer-linked proteins can then be immobilized on a functionalized surface of a **nanoparticle**. For example, aptamer-linked proteins can be attached covalently to a **nanoparticle** end-cap or to an exterior **nanoparticle** surface, including attachment of the aptamer-linked protein by functionalization

of the surface. Alternatively, aptamer-linked proteins can be covalently attached to a nanoparticle surface via linker molecules. Non-covalent linkage provides another method for introducing aptamer-linked proteins to a nanoparticle surface. For example, an aptamer-linked protein may be attached to a nanoparticle surface...

...by the SCE-detecting means affects the release of the surrogate marker from the nanoparticle. Because the surrogate marker is released from the nanoparticle only in the presence of an SCE, detection of the surrogate marker in a bodily...

...for Detecting Specific Chemical Entities (SCEs)

A nanostructure-based assembly of the invention comprises a nanoparticle, which contains a means for detecting a target SCE, a surrogate marker,

and, in c...

...peptides, RNA or DNA aptamers, cellular reporters or cellular ligands, can be attached to a nanoparticle surface to provide a means for vectoring the nanostructure-based assembly to a target SCE. Such SCE-detecting means may be covalently attached to the nanoparticle surface. In certain related embodiments, SCE detecting means are attached to a nanoparticle surface via linker molecules. SCE detecting means can also be attached to a nanoparticle surface by non-covalent linkage, for example, by absorption via hydrophobic binding or Van der...

...between the antibody and that of the target SCE. Antibodies can be attached to the nanoparticle using methods known to the skilled artisan.

Alternatively, recombinant bispecific antibody (bsFv) molecules can be...

...alleviation of a disease.

By way of example, one embodiment of the present invention uses nanoparticle-based assemblies that contain anti-oxidant genes (MnSOD, HO-1, and PON1) as the payload... Use
In one embodiment, a patient suffering from heroin addiction is administered a composition comprising nanoparticle-based assemblies of the invention. The nanoparticle-based assemblies are designed to detect the drug heroin. In one embodiment, the nanoparticle-based assemblies contain a nanoparticle, a surrogate marker, and an SCE-detector. Preferably, the SCE-detector is an aptamer that...

...and the surrogate marker (heroin-surrogate marker) are attached to a surface of the nanoparticle.

In a preferred embodiment, the heroin-aptamer is attached to an end-cap of a hollow nanoparticle that contains therein the heroin-surrogate marker. The heroin-aptamer is designed so that upon interaction with heroin, the end-cap is released from the nanoparticle to release the heroin-surrogate marker. The heroin-surrogate marker is readily detectable in bodily fluid samples taken from the patient.

To test for heroin use, the nanoparticle-based assemblies are administered to the patient and then a sample of the patient's...

...another embodiment of the invention, a patient suffering from atherosclerosis is administered a composition comprising nanoparticle-based assemblies to diagnose and treat atherosclerosis. The

nanoparticle -based assembly comprises a nanoparticle ; a surrogate marker; a payload; and an SCE-detector.

Treatment of atherosclerosis (payload) comprises anti...

...Glycogen Storage Disorder

Glycogen is readily detectable-, in bodily fluids (i.e., blood) using a nanoparticle -based assembly of the invention. According to the present invention, the nanoparticle -based assembly comprises a nanoparticle , a surrogate marker, and an SCE-detector that is designed to bind to the glycogen...

Claim

... disease, or disorder, comprising:

(a) administering to a patient a composition comprising at least one nanoparticle -based assembly, wherein the nanoparticle -based assembly comprises a nanoparticle ; a surrogate marker, and a means for detecting a specific chemical entity (SCE);
I 0...

...and biopsy samples.

I 0

8 The method according to claim 1, wherein the SCE- detecting means has a specific action on compounds selected from the group consisting of acet-aldehyde, acetone, ammonia , carbon monoxide, chloroform, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, o-toluidine, pentane sulfides and sulfides, H₂S...

...Human Chorionic Gonadotropin (b HCG. 1 1. The method according to claim 1, wherein the nanoparticle is formed with an interior void that contains the surrogate marker, wherein the nanoparticle has at least one open end to provide access to the interior void.

12 The...

...void also contains a payload.

13 The method according to claim I 1, wherein the nanoparticles further includes an end-cap to block the open end.
5

14 The method according...

...15 The method according to claim 13, wherein the end-cap is attached to the nanoparticle by covalent bonds.

16 The method according to claim 13, wherein the nanoparticle is in the form of a tubular body; and wherein the SCE-detecting means is attached to the end-cap.

17 The method according to claim 1, wherein the nanoparticle is composed of silica.

18 The method according to claim 1, wherein the nanoparticle is composed of a polymer.

19 The method according to claim 18, wherein the SCE-detecting means is attached to a surface of the **nanoparticle** using copolymerization.

20 The method according to claim 18, wherein the polymer **nanoparticle** is composed of polymers selected from the group consisting of polystyrene, polyorganosiloxane, poly(methyl methacrylate...

...occurring biopolymers.

I 0

2 1. The method according to claim 18, wherein the polymer **nanoparticle** is composed of biodegradable polymers selected from the group consisting of poly(caprolactone), poly(glycolic...

...polyhydroxycellulose, chitin, chitosan, and copolymers.

22 The method according to claim 18, wherein the polymer **nanoparticle** is composed of biocompatible polymers selected from the group consisting of poly(lactide-co-glycolide...

...The method according to claim 1, wherein the SCE-detecting means is incorporated into the **nanoparticle** .

24 The method according to claim 1, wherein the **nanoparticle** is produced in a shape selected from a group consisting of spherical; elliptical; cubic; cylindrical...

...irregular-prismatic; icosahedral; and cubo-octahedral.

25 The method according to claim 1, wherein the **nanoparticle** has a dimension less than 500 nm.

26 The method according to claim 1, wherein the surface of the **nanoparticle** is stealthy.

27 A method for diagnosis and treatment of a condition, disease, or disorder, comprising:

(a) administering to a patient a composition comprising at least one **nanoparticle** -based assembly, wherein the **nanoparticle** -based assembly comprises a **nanoparticle** ; a surrogate marker, a means for detecting a specific chemical entity (SCE), and a payload...

...the presence of the surrogate marker.

28 The method according to claim 27, wherein the **nanoparticle** is a nanotube.

29 The method according to claim 27, wherein SCE-detecting means is...

...and biopsy samples. 1 5 34. The method according to claim 27, wherein the SCE- detecting means has a specific action on compounds selected from the group consisting of acetaldehyde, acetone, ammonia , carbon monoxide, chloroform, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, o-toluidine, pentane sulfides and sulfides, H₂S...

...Beta Human Chorionic Gonadotropin (b HCG).

37 The method according to claim 27, wherein the **nanoparticle** is formed

with an interior void that contains the surrogate marker, wherein the **nanoparticle** has at least one open end to provide access to the interior void.

38 The...

...also contains 1 5 a payload.

39 The method according to claim 37, wherein the **nanoparticles** further includes an end-cap to block the open end.

40 The method according to...

...41 The method according to claim 39, wherein the end-cap is attached to the **nanoparticle** by covalent bonds.

42 The method according to claim 39, wherein the **nanoparticle** is in the form of a tubular body; and wherein the SCE-detecting means is attached to the end-cap.

43 The method according to claim 27, wherein the **nanoparticle** is composed of silica.

44 The method according to claim 27, wherein the **nanoparticle** is composed of a polymer.

45 The method according to claim 44, wherein the SCE-detecting means is attached to a surface of the **nanoparticle** using copolymerization.

46 The method according to claim 44, wherein the polymer **nanoparticle** is composed of polymers selected from the group consisting of polystyrene, polyorgaliosiloxane, poly(methyl methacrylate...

...naturally 1 5 occurring biopolymers.

47 The method according to claim 44, wherein the polymer **nanoparticle** is composed of biodegradable polymers selected from the group consisting of poly(caprolactone), poly(glycolic...

...polyhydroxycellulose, chitin, chitosan, and copolymers.

48 The method according to claim 44, wherein the polymer **nanoparticle** is composed of biocompatible polymers selected from the group consisting of poly(lactide-co-glycolide...

...The method according to claim 27, wherein the SCE-detecting means is incorporated into the **nanoparticle** .

50 The method according to claim 27, wherein the **nanoparticle** is produced in a shape selected from a group consisting of spherical; elliptical; cubic; cylindrical...

...irregular-prismatic; icosahedral; and cubo-octahedral.

51 The method according to claim 27, wherein the **nanoparticle** has a dimension less than 500 nm.

52 The method according to claim 27, wherein the surface of the

nanoparticle is stealthy.

53 The method according to claim 27, wherein the payload is selected from
...

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SELF-ASSEMBLING NANOPARTICLE CONJUGATES
CONJUGUES NANOPARTICULAIRES A AUTO-ASSEMBLAGE

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SELF-ASSEMBLING NANOPARTICLE CONJUGATES
CONJUGUES NANOPARTICULAIRES A AUTO-ASSEMBLAGE

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Detailed Description

Claims

English Abstract

This invention relates to magnetic nanoparticle conjugates and related
compositions and methods of use.

French Abstract

L'invention concerne des conjugues nanoparticulaires magnetiques et des
compositions relatives et des procedes d'utilisation de ceux-ci.

Detailed Description

Self-Assembling Nanoparticle Conjugates

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of United States Provisional...

...which is incorporated by reference in its entirety.

TECHNICAL FIELD

This invention relates to magnetic nanoparticle conjugates and related compositions and methods of use.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

The work...

...their effects on water relaxation rate are

I

unspecified and not relevant to their application. Nanoparticles do not respond

to the weak, magnetic fields of hand held magnets. Thus, biocompatible nanoparticles with unique optical and/or magnetic properties could have in vitro and in vivo diagnostic applications. The ability to image specific enzyme activities using such nanoparticles would have applications for detecting a variety of diseases and evaluating targeted therapies in individual patients.

SUMMARY

This invention relates to magnetic nanoparticle conjugates and related compositions and methods of use.

In one aspect this invention relates to compositions having at least two 1 5 nanoparticle conjugates, each nanoparticle conjugate having a magnetic nanoparticle ; and at least one substrate moiety, in which each substrate moiety is linked to the nanoparticle and is chemically modified when the conjugate interacts with a target enzyme. When the target enzyme is absent, the nanoparticle conjugates are essentially monodisperse in liquids; and when the target enzyme is present, the nanoparticle conjugates self-assemble into one or more nanoparticle conjugate clusters through the formation of intermolecular linkages between the chemically modified substrate moieties.

Embodiments...

...which n is 0- 1 00, e.g., n can be 6) that link the nanoparticle to one or more substrate moieties.

The magnetic nanoparticles each can include a magnetic metal oxide (e.g., a superparamagnetic metal oxide). The metal oxide can be iron oxide. In some embodiments, the nanoparticles can be amino-derivatized cross-linked iron oxide nanoparticles .

The substrate moieties can include a phenolic moiety, and can be chemically modified by oxidation...

...protease or a peroxidase (e.g., a myeloperoxidase or horseradish peroxidase).

Each of the monodisperse nanoparticle conjugates can have an average particle size of between about 40 nm and about 60 nm. In some embodiments,

each of the monodisperse nanoparticle conjugates can have an average particle size of about 50 nm.

Each of the nanoparticle conjugate clusters can have an average particle size of between about 400 nm and about 500 nm. In some embodiments, each of the nanoparticle conjugate clusters can have an average particle size of about 10 to 450 nm.

Each of the monodisperse nanoparticle conjugates can have an RI relaxivity between about 5 and 30 mM⁻¹ sec⁻¹...

...of intermolecular linkages between the chemically modified substrate moieties can result in crosslinking of the nanoparticle Conjugates.

The composition can further include a fluid media. Self-assembly of the nanoparticle conjugates can result in the spin-spin relaxation time of the fluid being decreased relative to the spin-spin relaxation time of the fluid having essentially only monodisperse nanoparticle conjugates present. The decrease in spin-spin relaxation time can be dependent upon the concentration of the target enzyme.

The nanoparticle conjugate can have a formula X-(L)_x-A, in which X is a magnetic nanoparticle; L is -NH-, -NHCO(CH₂), C(O)-, -C(O)O-, or -SS-, in which n...

...N

H

In some embodiments, the composition can include a population of at least two nanoparticle conjugates, in which at least one nanoparticle conjugate has a magnetic nanoparticle and/or substrate moiety that is different from the magnetic nanoparticle and/or substrate moiety of one or more members in the population. For example, a population can include one or more first nanoparticle Conjugates, each including a first magnetic nanoparticle and a first substrate moiety, and one or more second nanoparticle conjugates, each including a second magnetic nanoparticle and a second substrate moiety, whereby two types of nanoparticle conjugates are present. The first and second magnetic nanoparticles can be different and/or the first and second substrate moieties can be different...

...sample, the method includes (i) providing a composition including at least two of the new nanoparticle conjugates described herein; (ii) contacting the composition with a fluid sample; (iii) allowing time (a) for the target enzyme to contact the nanoparticle conjugates and (b) for the

4

nanoparticle conjugates to self-assemble into clusters through the formation of intermolecular linkages between the chemically...

...by (i) administering to the subject a composition including at least two of the new nanoparticle conjugates described herein; (ii) allowing time (a) for the target enzyme to contact the nanoparticle conjugates and (b) for the nanoparticle conjugates to self-assemble into clusters

through the formation of intermolecular linkages between the chemically
...

...need of such detection.

In one aspect, this invention relates to the new self-assembling,
nanoparticle conjugates having a magnetic nanoparticle ; and at least
one
substrate moiety, in which each substrate moiety is linked to the
nanoparticle and is chemically modified when the conjugate interacts
with a target enzyme.

When two or more nanoparticle conjugates are present and when the
target
enzyme is absent, the nanoparticle conjugates are essentially
monodisperse in a liquid; and when two or more nanoparticle conjugates
are present and when the target enzyme is present, the nanoparticle
conjugates self-assemble into one or more nanoparticle conjugate
clusters through the formation of intermolecular linkages between the
chemically modified substrate moieties.

In...

...have a formula $X-(L)_x-A$, in
which in which X is a magnetic nanoparticle ; L is -NH-, -NHC(O)-,
NHC(O)(CH₂)_nC(O)-, -C(O)O-, or -SS...

...relates to a packaged product including a composition having at least
two of the new nanoparticle conjugates described herein.

Embodiments may include one or more of the following advantages.

In all embodiments, the nanoparticle conjugates are essentially
monodispersed in the absence of a target enzyme, which can reduce the...

...profiles that can sometimes be associated with multi-particle
preparations.

6

In some embodiments, the nanoparticle conjugates contain phenolic
moieties as substrate moieties, in which relatively straightforward
substitutions of the aromatic...

...of target enzyme specific
conjugates can be readily designed and prepared from the same basic
nanoparticle scaffold.

In some embodiments, a single enzyme can result in the self-assembly of
a plurality of nanoparticle conjugates, thereby achieving biological
amplification at relatively low nanoparticle conjugate concentrations.

In some embodiments, preferential changes in R₂ relaxivity can allow R₁
relaxivity/R₂...

...is a graphical representation of the particle size distribution by light
scattering of the dopamine nanoparticle conjugates before incubation
with horse radish peroxidase (HRP).

FIG. 1 B is a graphical representation of the particle size distribution
by light scattering of the dopamine nanoparticle conjugates after
incubation with HRP.

7

FIG. 2 is a graphical representation of the effects of increasing HRP concentration on the M of a solution containing dopamine **nanoparticle** conjugates with (solid squares) and without (solid triangles) hydrogen peroxide.

FIG. 3 is a graphical...

...increasing the amount of sodium azide (inhibitor) on the M of a solution containing dopamine **nanoparticle** conjugates with hydrogen peroxide.

FIG. 4A is a graphical representation of 6T2 values of the serotonin **nanoparticle** conjugates in the presence of increasing amounts of myeloperoxidase detected using a 1.5T clinical...

...magnetic resonance image (1.5T MRI) of myeloperoxidase activity (0 units/[tL MPO) using doparnine- **nanoparticle** conjugates. There was essentially no difference in signal intensity observed between this image and the...

...resonance image (1.5T MRI) of myeloperoxidase activity (0.0061 units/@LL MPO) using doparnine- **nanoparticle** conjugates. There was essentially no difference in signal intensity observed between this image and the...

...resonance image (1.5T MRI) of myeloperoxidase activity (0.025 units/@tL MPO) using doparnine- **nanoparticle** conjugates. There was essentially no difference in signal intensity observed between this image and the...

...magnetic resonance image (1.5T MRI) of myeloperoxidase activity (0 units/@tL MPO) using serotonin- **nanoparticle** conjugates. There was essentially no difference in signal intensity observed between this image and the...

...resonance image (1.5T MRI) of myeloperoxidase activity (0.0061 units/@tL MPO) using serotonin- **nanoparticle** conjugates.

FIG. 5F is a magnetic resonance image (1.5T MRI) of myeloperoxidase activity

9

(0.025 units/@tL, MPO) using serotonin- **nanoparticle** conjugates.

FIG. 5G is a T2 (nise) magnetic resonance image signal intensity level scale corresponding...

...in the various drawings indicate like elements.

DETAILED DESCRIPTION

General

This invention relates to magnetic **nanoparticle** conjugates and related compositions and methods of use. The **nanoparticle** conjugates generally include a magnetic **nanoparticle** (circled "NP" in Scheme I below), that is linked to at least one substrate moiety (circled "S" in Scheme 1 below). The **nanoparticle** conjugates may optionally contain functional

groups that link one or more substrate moieties to the **nanoparticle**. The substrate moiety can be any chemical group that can participate in an enzyme (e.g., a target enzyme)-mediated chemical reaction. As such, one or more **nanoparticle**-bound substrate moieties can be chemically modified (shaded circled "S" in Scheme I below) upon...

...peroxidase, a protease). When the target enzyme interacts with a population of two or more **nanoparticle** conjugates, the conjugates can self-assemble into **nanoparticle** conjugate clusters through the formation of intermolecular (i.e., interconjugate) linkages between the chemically modified substrate moieties. In the absence of a target enzyme, the **nanoparticle** conjugates are essentially monodispersed (e.g., in solution or in a nonhomogenous fluid media).

Scheme I

enzyme

----- 10

10

In general, the clusters formed from the **nanoparticle** conjugates described herein have one or more measurable properties (e.g., magnetic properties), that are...

...increased or decreased) relative to the same one or more measurable properties of the monodispersed **nanoparticle** conjugates. For example, the solvent (e.g., water) spin-spin relaxation times T_2 for solution phase **nanoparticle** conjugate clusters are relatively low in magnitude and differentiable, (e.g., by nuclear magnetic resonance...

...from the relatively high solvent spin-spin relaxation times for the corresponding monodispersed, solution phase **nanoparticle** conjugates. Accordingly, it is believed that solvent spin-spin relaxation times can be a useful parameter for determining the presence or absence of a target enzyme in biological samples containing **nanoparticle**

conjugates with target enzyme-specific substrate moieties. While not wishing to be bound by theory...

... T_2 would be observed in samples containing the target enzyme because interaction of the monodispersed **nanoparticle** conjugates (high T_2) with the target enzyme results in the formation of one or...

...respectively.

The term "interacts" refers to any contact, reaction, or binding that occurs between a **nanoparticle** conjugate and a target enzyme.

It is understood that the actual electronic structure of some...

...predominant resonance forms for a particular species.

14

Structure of Nanoparticle Conjugates

In all embodiments the **nanoparticle** component of the conjugate is a magnetic **nanoparticle**, (e.g., magnetic metal oxide, such as superparamagnetic iron oxide). The magnetic metal oxide can...

...magnetic susceptibility such as

superparamagnetic compounds and magnetite, gamma ferric oxide, or metallic iron. Preferred **nanoparticles** include those having a relatively high relaxivity, i.e., strong effect on water relaxation.

In all embodiments, at least one substrate moiety is covalently linked to the **nanoparticle**. In some embodiments, the substrate moiety is linked to the **nanoparticle** via a functional group. The functional group can be chosen or designed primarily on factors...

...alkylene linker portion, $(CH_2)_n$, may also be used to attach substrate moieties to the **nanoparticle**. In some embodiments, the functional group is $-NHQO(CH_2)_6QO-$. The functional group may be present on a starting material or synthetic intermediate that is associated with either the **nanoparticle** or the substrate moiety.

The number of substrate moieties linked to a **nanoparticle** may be selected as desired. In some embodiments, a **nanoparticle** starting material can contain one or more functional groups for attachment of substrate moieties, (e...

...or 50 functional groups). The number of substrate moieties that are ultimately linked to the **nanoparticle** can either be equal to or less than the number of functional groups that are available for attachment to the **nanoparticle**. In some embodiments, the number of substrate
15
moieties linked can correspond to a number...

...deten-nivative of the number of substrate moieties that are ultimately loaded on to the **nanoparticle**. In any event, it is permissible for 10 the number of substrate moieties per **nanoparticle** conjugate to vary within a given population of two or more **nanoparticle** conjugates.

The substrate moiety can generally be any chemical group that (1) can function as...al. J Biol Chem 1998, 273, 32030-32037).

17

Scheme 2

OH OH OH OH

Accordingly, **nanoparticle** conjugates having phenolic substrate moieties
10 (Structure I in Scheme 3 below) can be useful...

...magnetic resonance signal.

18

Scheme 3

HO' Om

HO,@o ON H

One subset of **nanoparticle** conjugates has a formula $X-(L)_x-A$, in which.

X is a magnetic **nanoparticle** ;

L is a functional group that may include $-NH-$, $-NHC(O)-$,
 $N-HC(O)(CH_2...$

...or 1.

A useful subset includes those conjugates in which X is an iron oxide
nanoparticle, x is 1, L is $-NHC(O)(CH_2)_6C(O)-$, and A is an alkylamino
substituted...

...N N NH

H H 1-40

D

In general, the overall size of the **nanoparticle** conjugates is about 15 to 200 nm, e.g., about 20 to 100 nm, about...

...of the particle, e.g., greater than 15, 20, 25 or 30 percent.

Synthesis of **Nanoparticle** Conjugates

In some embodiments, **nanoparticles** having functional groups, (e.g., electrophilic functional groups such as carboxy groups or nucleophilic groups

20

such as amino groups) can be employed as starting materials for the **nanoparticle** conjugates.

Carboxy functionalized **nanoparticles** can be made, for example, according to the method of Gonnar (see WO 00/61191...

...salts are mixed together and are then neutralized with ammonium hydroxide. The resulting carboxy functionalized **nanoparticles** can be used for coupling amino functionalized groups, (e.g., a further segment of the functional group or the substrate moiety).

Carboxy-functionalized **nanoparticles** can also be made from polysaccharide coated **nanoparticles** by reaction with bromo or chloroacetic acid in strong base to attach carboxyl groups. In addition, carboxy-functionalized particles can be made from amino-functionalized **nanoparticles** by converting amino to carboxy groups by the use of reagents such as succinic anhydride or maleic anhydride.

Nanoparticle size can be controlled by adjusting reaction conditions, for example, by using low temperature during...

...centrifugation, ultrafiltration, or gel filtration, as described, for example in U.S. Patent No.

594925814.

Nanoparticles can also be synthesized according to the method of Molday (Molday, R.S. and D...

...52(3):353-67, and treated with periodate to form aldehyde groups. The aldehyde-containing **nanoparticles** can then be reacted with a diamine (e.g., ethylene diamine or hexanediamine), which will form a Schiff base, followed by reduction with sodium borohydride or sodium cyanoborohydride.

Dextran-coated **nanoparticles** can be made and cross-linked with epichlorohydrin. The addition of ammonia will react with epoxy groups to generate amine groups, see Flogernann, D., et al., Improvement of MRI probes to allow efficient detection of gene expression Bioconjug. Chem. 2000. 11(6):9416, and Josephson et al., "High-efficiency intracellular...

...when functionalized with amine is referred to as amine-CLIO or NH₂-CLIO.

Carboxy-functionalized **nanoparticles** can be converted to

amino functionalized magnetic particles by the use of water-soluble carbodiimides and...

...corresponding to C and D were prepared using amino functionalized dextran-caged superparamagnetic iron oxide nanoparticles were used as the starting material. Dopamine or serotonin was conjugated to the aminated magnetic nanoparticles using suberic acid bis(N-hydroxysuccinimide ester) (DSS, Pierce Co). On average, each nanoparticle starting material had about 40 reactive amino groups, which were used for conjugation. Serotonin attachment was verified through its fluorescent emission at 345 nm. These nanoparticle conjugates were monodispersed in solution, having a narrow particle size distribution as determined by light...

...an average particles size of about 50 nm. Particle size distribution for the dopamine-containing nanoparticle conjugates is shown in FIG. 1A. The water protons' spin-lattice relaxation (R_1) of the nanoparticle conjugates was 25.8 s/M-1 while the spin-spin relaxation (R_2) was 67...

...in, for example, Shen, T., et al. Magn. Reson. Med. 29, 599
Uses of the Nanoparticle Conjugates
Solvent, (e.g., water), spin-spin relaxation times (T_2) can be determined by relaxation...

...D., et al. Bioconjug Chem 2002, 13, 116-121.
In some embodiments, the magnetic nanoparticle conjugates self-assemble in solution by the action of a specific peroxidase, with the enzyme mediated magnetic nanoparticle self-assembly acting as a magnetic resonance signal amplification system, which is sensitive to the...

...dopamine and serotonin were selected and used as substrate moieties in two separate sets of nanoparticle conjugates (e.g., C and D) for detection of HRP and MPO, respectively. These phenolic...

...a suitable nucleic acid vector introduced into the tissue.

To test whether incubation of the nanoparticle conjugates with the corresponding peroxidase would result in cluster formation, the dopamine-nanoparticle conjugates (IO-1) were...

...continue growing in size and did not precipitate. Similar results were observed when serotonin-nanoparticles were incubated with myeloperoxidase.

Next, we investigated whether the peroxidase-mediated clustering would result in...

...time changes (Δ) of the solution. For these experiments, a solution of the HRP targeting nanoparticle conjugate (10 μ M, 0.1 M phosphate pH 6.0) was incubated...

...nanoparticle conjugates can be used as nanosensors for peroxidase activity detection.

The ability of the nanoparticle conjugates to image myeloperoxidase (MPO) activity was tested using a 1.5T clinical MRI imaging...

...J. W.; Libby, P. Am J Pathol 2001, 158, 879-89 1).

A serotonin-containing **nanoparticle** conjugate (prepared as described herein) was selected for the MPO imaging experiments because serotonin has...

...386; Dunford, H. B.; Hsuanyu, Y. Biochem Cell Biol 1999, 77, 449-457). The serotonin- **nanoparticles** (3@tg Fe/mL, OAM phosphate pH 6.0)

were incubated with various amounts of...

...FIGS. 4I-4J and 4J). Likewise, as shown in FIGS. 5A-5G, the dopamine-containing **nanoparticle** conjugates did not show any 6T2 in the presence of MPO (i.e., essentially no difference in signal intensity observed when dopamine- **nanoparticle** conjugates are incubated with myeloperoxidase). The findings demonstrate that the selectivity of the particle-bound...

...of chemical bonds via 30 different reaction mechanisms.

In magnetic resonance (MR) imaging applications, the **nanoparticle** conjugates can be used in methods for the detection and a spatial localization of target...

...target enzymes in vivo.

25

The new conjugates are essentially nontoxic to mammalian cells. The **nanoparticle** conjugates can be administered to a subject, e.g., a human or animal, such as...

...inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir). Compositions containing the **nanoparticle** conjugates of this invention may contain any conventional non-toxic pharmaceutically-acceptable carriers, adjuvants or ...

...selectivity for one or more target enzymes. For example, libraries of phenolic substrates attached to **nanoparticles** can be screened by high throughput NMR methods described herein (e.g., for numerous peroxidases ...

Claim

I . A composition comprising at least two **nanoparticle** conjugates, each **nanoparticle** conjugate comprising:
a magnetic **nanoparticle** ; and
at least one substrate moiety, in which each substrate moiety is linked to the **nanoparticle** and is chemically modified when the conjugate interacts with a target enzyme; wherein,
when the target enzyme is absent, the **nanoparticle** conjugates are essentially monodisperse in a liquid; and
when the target enzyme is present, the **nanoparticle** conjugates selfassemble into one or more **nanoparticle** conjugate clusters through the formation of intermolecular linkages between the chemically modified substrate moieties.

2...

...composition of claim 1, wherein the the conjugates further comprise functional groups that link the nanoparticle to one or more substrate moieties.

3 The composition of claim 2, wherein the functional...

...sulfhydryl groups,
wherein n is 0

4 The composition of claim 1, wherein the magnetic nanoparticles each comprise a magnetic metal oxide.

5 The composition of claim 4, wherein the magnetic...

...wherein the metal oxide is iron
oxide.

7 The composition of claim 4, wherein the nanoparticles are an amino-derivatized cross-linked iron oxide nanoparticles .

27

8 The composition of claim 1, wherein the substrate moieties comprise a phenolic moiety...

...peroxidase is
horseradish peroxidase.

15 The composition of claim 1, wherein each of the monodisperse nanoparticle conjugates has an average particle size of between about 40 nm and about 60 tim.

16 The composition of claim 1, wherein each of the monodisperse nanoparticle conjugates has an average particle size of about 50 nin.

17 The composition of claim 1, wherein each of the nanoparticle conjugate clusters has an average particle size of between about 400 mu and about 500 mu.

18 The composition of claim 1, wherein each of the nanoparticle conjugate clusters has an average particle size of about 450 run.

28

19 The composition of claim 14, wherein each of the monodisperse nanoparticle conjugates has an RI relaxivity between about 5 and 30 mM-1 sec-,
I I...

...nation of
intermolecular linkages between the chemically modified substrate moieties results in crosslinking of the nanoparticle conjugates.

24 The composition of claim 1, wherein the composition further comprises a fluid media.

25 The composition of claim 24, wherein self-assembly of the nanoparticle conjugates results in the spin-spin relaxation time of the fluid being decreased relative to the spin-spin relaxation time of the fluid having essentially only monodisperse nanoparticle conjugates present.

26 The composition of claim 24, wherein the decrease in spin-spin

relaxation...

...upon the concentration of the target enzyme.

27 The composition of claim 1, wherein the **nanoparticle** conjugate has a fori-nula

X-(L)x-A, wherein:

X is a magnetic **nanoparticle** ;

29

L is -NH-, -NHC(O)(CH₂)_nC(O)-, -C(O)O-, or -SS-, wherein...

...enzyme

in a sample, the method comprising:

(i) providing a composition comprising at least two **nanoparticle** conjugates, each **nanoparticle** conjugate comprising a magnetic **nanoparticle** ; and at least one substrate moiety, in which each substrate moiety is linked to the **nanoparticle** and is chemically modified when the conjugate interacts with a target enzyme; wherein, when the target enzyme is absent, the **nanoparticle** conjugates are essentially monodisperse; and when the target enzyme is present, the **nanoparticle** conjugates self-assemble into one or more **nanoparticle**

conjugate clusters through the formation of intermolecular linkages between the

chemically modified substrate moieties;

(ii...

...with a fluid sample;

(iii) allowing time (a) for the target enzyme to contact the **nanoparticle** conjugates and (b) for the **nanoparticle** conjugates to self-assemble into clusters through the formation of intermolecular linkages between the chemically...

...subject, the method comprising:

(i) administering to the subject a composition comprising at least two **nanoparticle** conjugates, each **nanoparticle** conjugate comprising a magnetic **nanoparticle** ; and at least one substrate moiety, in which each substrate moiety is linked to the **nanoparticle** and is chemically modified when the conjugate

interacts with a target enzyme; wherein, when the target enzyme is absent, the **nanoparticle** conjugates are essentially monodisperse; and when the target enzyme is present, the **nanoparticle** conjugates self-assemble into one or more **nanoparticle** conjugate clusters through the formation of intermolecular linkages between the chemically modified substrate moieties;

(ii) allowing time (a) for the target enzyme to contact the **nanoparticle** conjugates and (b) for the **nanoparticle** conjugates to self-assemble into clusters through the formation of intermolecular linkages between the chemically...

...identifying the subject as being in need of such detection.

32

42 A self-assembling, **nanoparticle** conjugate comprising:

a magnetic **nanoparticle** ; and

at least one substrate moiety, in which each substrate moiety is linked to the **nanoparticle** and is chemically modified when the conjugate interacts with a

target enzyme; wherein,

when two or more **nanoparticle** conjugates are present and when the

target enzyme is absent, the nanoparticle conjugates are essentially monodisperse in a liquid; and
when two or more nanoparticle conjugates are present and when the
1 5 target enzyme is present, the nanoparticle conjugates self-assemble
into one or more nanoparticle conjugate clusters through the formation
of intermolecular linkages between the chemically modified substrate
moieties.

43 The nanoparticle conjugate of claim 42, wherein the conjugate
has a fon-nula X-(L)x-A,
wherein:

X is a magnetic nanoparticle ;

L is -NH-, -NHC(O)(CH₂),C(O)-, -C(O)O-, or -SS-, wherein n...

...CH₂CH₂NWL@

N

H

34

52 A packaged product comprising:

a composition comprising at least two nanoparticle conjugates, each
nanoparticle conjugate comprising:

a magnetic nanoparticle ; and

at least one substrate moiety, in which each substrate moiety is linked
to lo the nanoparticle and is chemically modified when the conjugate
interacts with a

target enzyme; wherein,

when the target enzyme is absent, the nanoparticle conjugates are
essentially monodisperse in a liquid; and

when the target enzyme is present, the nanoparticle conjugates
selfassemble into one or more nanoparticle conjugate clusters through
the formation of intermolecular linkages between the chemically modified
substrate moieties.

35

4/3,KWIC/21 (Item 4 from file: '349)

DIALOG(R)File 349:PCT FULLTEXT

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01249901 **Image available**

OPTICAL STORAGE MEDIUM HAVING AN ANALYTE CONTAINING POLYMER FILM, USE
THEREOF

SUPPORT D'ENREGISTREMENT OPTIQUE A FILM POLYMERES CONTENANT UN ANALYTE, ET
UTILISATION

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

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Detailed Description

Claims

Detailed Description

... weak and strong absorbing regions.

FIG. 9 is a graph depicting the response of three **sensor** regions as recorded using an optical drive. Different **sensor** regions were exposed to saturated **ammonia** vapor for different amounts of time ($t_1 < t_2 < 0$).

FIG. 10 is a graph illustrating changes in an optical signal of a **sensor** spot for detection of NH_4^+

DETAILED DESCRIPTION OF THE INVENTION

The present disclosure is directed...chemical and biological species.

Analyte-specific reagents include organic and inorganic dyes and pigments, nanocrystals, **nanoparticles**, quantum dots, organic fluorophores, inorganic fluorophores and similar materials.

Examples of organic compounds which can...

...645 -700

DDI -710 -745

IR125 -795 -840

DTTCI @760 -815

HDITCI -780 -825

CdSe **nanoparticles**, crystal diameter = 2.8 nm -520 -535

CdSe **nanoparticles**, crystal diameter = 3.4 nm @545 -560

CdSe **nanoparticles**, crystal diameter = 4.0 nm -575 -585

CdSe **nanoparticles**, crystal diameter = 4.7 nm -595 -610

CdSe **nanoparticles**, crystal diameter = 5.6 nm -625 -640

In other embodiments, non-fluorescing analyte-specific...

...birefringence changes when temperature increases.

As noted above, the analyte-specific reagents also include nanocrystals, **nanoparticles** and quantum dots and are known to those skilled in the-art. Suitable nanocrystals include, but are not limited to, those

made Of MOS2, ZnO, Si, CdTe, and Ge. Suitable **nanoparticles** include, but are not limited to, those made of Cu, SiO2, and LaB6.

Quantum dots...

...where a pH sensitive reagent such as bromothymol blue or bromocresol green is used, the **sensor** spot can be exposed to vapor or liquids which may include **ammonia** and the **sensor** read to confirm the presence of and the amounts of such an alkaline vapor. Such...exposure times from 0 to about 20 seconds . Figure 9 shows the response of three **sensor** regions as recorded using an optical drive (LG Electronics, Inc., Model GCC4480B) where different **sensor** regions were exposed to saturated **ammonia** vapor for different amounts of time (t, < t2 < t3)

EXAMPLE 4

For **detection** of ionic species in water such as NH4'-, thin film regions containing different pH dyes...

Claim

... analyte-specific reagent is selected from the group consisting of organic dyes, inorganic dyes, nanocrystals, **nanoparticles** , quantum dots, organic fluorophores, inorganic fluorophores, IR

40

absorbing dyes, near infrared absorbing materials, UV...

4/3,KWIC/22 (Item 5 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01245390 **Image available**

MINIATURIZED MULTI-GAS AND VAPOR SENSOR DEVICES AND ASSOCIATED METHODS OF FABRICATION

DISPOSITIFS DE DETECTION MINIATURISES POUR PLUSIEURS VAPEURS ET GAZ ET PROCEDES DE FABRICATION ASSOCIES

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO

RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LU MC NL PL PT
RO SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
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Fulltext Availability:

Detailed Description

Detailed Description

... the sensor device of Figure 1, highlighting

N

the addition of a thin film or **nanoparticle** layer to one or more cells
of the sensor

device;

Figure 3 is a cross...

...keeping

6

particulates and/or contaminants away from the one or more thin film or
nanoparticle
layers of Figure 2;

Figure 4 is a cross-sectional side view of one embodiment...

...fit different geometrical requirements for specific applications.

Referring to Figure 2, a thin film or **nanoparticle** layer 22 is added to
one or more cells 18 of the sensor device 10...

...12 opposite the corresponding thin film heater/thermometer 20.

Preferably, the thin

10

film or **nanoparticle** layer 22. has a thickness of between about 1 nm
and about 5 microns, although other suitable dimensions may be used. The
thin film or **nanoparticle** layer 22 consists of a zeolite thin film, a
suitable cross-linked organic polyelectrolyte, a...

...generate heat upon the physisorption of gasses and/or vapors.

Preferably, the thin film or **nanoparticle** layer 22 is nano-structured
(consisting of spheres, rods, hollow fibers, etc.) such that heat...

...thermometers 20, and not into the surrounding environment. In general,
because the thin film or **nanoparticle** layer 22 consists of a plurality
of nanopores, molecules are allowed to travel in and...

...undesirably increase the response time-of the sensor device 10. The
thin film or **nanoparticle** layer 22 acts as an interface between a
substance to be detected, present in one...

...of a given amount of this substance onto the surface of the thin film or
nanoparticle layer 22, a corresponding amount of heat is released. This
heat exchange is measured by...

...0. The adsorbate is driven out of the porous structure of the thin film
or **nanoparticle** layer 22 naturally as its partial pressure in the
environment drops. It is possible to accelerate desorption of the
adsorbate from the porous structure of the thin film or **nanoparticle**
layer 20. by pulse heating the thin film or **nanoparticle** layer 22

without damaging its structure.

Preferably, the microstructure of the thin film or **nanoparticle** layer 22 and its pore dimensions are customized to ensure the high selectivity of the...

...sensing thin film
heater/thermometer 20 due to heat exchange with the thin film or **nanoparticle** layer 22.

Referring to Figure 3, in an alternative embodiment of the invention, the sensor...

...protection mechanism designed to prevent the "locking" of the pores of the thin film or **nanoparticle** layer 22. In general, the sensor device 10 described above is disposed directly adjacent to...
...grid 32 operable for keeping particulates and/or contaminants away from the thin film or **nanoparticle** layer 22. The grid 32 may be fabricated using standard silicon processing and lithography techniques...
...1-3) of the invention require short heat transfer paths between the thin film or **nanoparticle** layer(s) 22 (Figures 2 and 3) and the thin film heater/thermometer(s) 20...
...may be used to keep particulates and/or contaminants away from the thin film or **nanoparticle** layer 22. Preferably, the volume 42 of the recessed cavity 40 surrounding the sensor device...
...that will subsequently be deposited (about 0.5 microns). The image is reversed using an **ammonia** diffusion bake, flood exposure, and development of the photoresist (PR).

Referring to Figure 8, the fourth step in the fabrication of the **sensor** device 10 includes evaporating a metal layer 58 onto the surface of the photoresist...

...18

14

(Figures 1 and 2) described above. At this point, the thin film or **nanoparticle** layer 22 (Figure 2) may be deposited or grown directly on the surface of the...

4/3,KWIC/23 (Item 6 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01233744 **Image available**

HIGH SURFACE AREA MATERIAL BLENDS FOR ODOR REDUCTION, ARTICLES UTILIZING SUCH BLENDS AND METHODS OF USING SAME

MELANGES DE SUBSTANCES A SURFACE ACTIVE ELEVEE DESTINES A LA REDUCTION D'ODEUR, ARTICLES METTANT EN OEUVRE DE TELS MELANGES ET PROCEDES D'UTILISATION DE CEUX-CI

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DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

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Detailed Description

Claims

Detailed Description

... reducing or removing) gases and/or odorous compounds. The high surface
area materials, such as **nanoparticles**, may be utilized in their
unmodified state or modified by being associated with metal components...

...product within an enclosure formed by the packaging material; and a
blend of differently modified **nanoparticles** contained within

3

the packaging material enclosure, whereby as odor or gas is generated
within the enclosure, it is adsorbed onto the surfaces of the
nanoparticle blend.

In still a-further alternative embodiment, a package containing a product
includes a product...

...within an enclosure formed by the packaging material; and a blend of
modified and unmodified **nanoparticles** contained within the packaging
material enclosure; whereby, as odor or gas is generated within the
enclosure, it is adsorbed onto the surfaces of the **nanoparticle** blend.

In still a further alternative embodiment a method for neutralizing odor
contained within the...

...an enclosure formed by the packaging material; and a blend of either
modified and unmodified **nanoparticles**, differently modified
nanoparticles, different unmodified **nanoparticles** or a combination
thereof with blend contained within the packaging material enclosure. As
odor or...

...DRAWINGS

Fig. 1 is a drawing of a modified high surface area material,
specifically a **nanoparticle** of the inventive composition, in accordance
with one embodiment of this invention.

Fig. 2 is...

...many different odorous categories. Therefore, by using a blend of high surface area materials, particularly **nanoparticles**, and desirably silica **nanoparticles** in product

4

packaging, various odor causing chemicals can be adsorbed/absorbed on the **nanoparticle** surfaces, resulting in reduced product odor. In particular, by blending unmodified **nanoparticles** with metal modified **nanoparticles**, or alternatively, blending various different metal modified **nanoparticles**, a targeted odor reducing composition can be formulated.

For the purposes of this application, the terms "unmodified" and "nonmodified" are used interchangeably to mean a **nanoparticle** that has not been modified to have at least one metal component (such as metal...

...of this application, the terms "metal modified" and "metallized" are used interchangeably to mean a **nanoparticle** that has been modified to have at least one metal component (such as metal ion) associated with it. By being "associated" the metal component is in close proximity to the **nanoparticle** such as through charge attraction or other more secure bonding methods. In a desirable embodiment, such metal component is not easily dislodged from its association with the **nanoparticle**.

Often, product odors are not caused by single odor causing chemicals, but instead are caused...

...of multiple odor causing chemicals. Therefore, by using a blend combination of different modified metallized **nanoparticles** and/or metallized **nanoparticles** and unmodified **nanoparticles**, targeted odor reduction can be achieved for specific product applications. For example, the metal modified **nanoparticles** would be effective for neutralizing bathroom odors (sulfides and amines) whereas, unmodified **nanoparticles** would be more effective for neutralizing tobacco odor (aliphatic acids and aldehydes). Further still, a blend of modified and unmodified **nanoparticles** would be a desirable composition for cooking food (kitchen) odors (aldehydes, sulfides and amines).

Such...

...or in a surrounding environment.

By reacting various transition metals onto the surface of the **nanoparticles**, the affinity for adsorbing various odor causing chemicals can be changed. The blended **nanoparticles** may then be added to the product packaging, either as an insert, as part of...

...has been found that the use of blended high surface area materials, and in particular, **nanoparticles**, applied to either an insert within the package, the product within the package or to...

...In a desirable embodiment, this invention specifically relates to high surface area materials, such as **nanoparticles**, which have been modified with at least one metal ion.

Blends of the differently modified **nanoparticles**, or modified **nanoparticles** and unmodified particles may then be used to adsorb odors in product packaging headspace. It...

...gram, and even more suitably at least about 800 square meters/gram.

As previously indicated, " nanoparticles " are examples of high surface area materials useful in this invention. For the purposes of this application, the term " nanoparticle " refers to a high surface material having an effective particle diameter of less than about 500 nanometers. While the invention will be described hereinafter with particular reference to nanoparticles , it will be understood that the invention is useful with various high surface area materials.

Fig. 1 shows a modified nanoparticle 10 according to one embodiment of this invention, useful as a gas and/or odor removing particle. The modified nanoparticle 10 includes a nanoparticle 15 and metal ions 20. While Fig. 1 shows a plurality of metal ions 20, modified nanoparticle 10 can have various amounts of metal ions 20 and will have at least one metal ion 20. The modified nanoparticle 10 is useful for removing various gaseous compounds and/or odorous compounds. The specific compound...

...removed is generally dependent on the specific metal ions 20 used and the type of nanoparticle 15.

The modified nanoparticle may adsorb odors or gas by attraction of odor or gas materials 30 to the metal ions, or alternatively, directly to the surface of the nanoparticle 40.

7

Nanoparticles useful in this invention include, without limitation, silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold, zinc oxide, copper oxide, organic nanoparticles such as polystyrene, and combinations thereof. Nanoparticles are not generally ionic yet still have an overall electric Zeta Potential. "Zeta Potential" refers...

...electrical potential, or electrokinetic potential, that exists across the interface of all solids and liquids. Nanoparticles with either positive or negative Zeta Potentials are known. Naturally occurring chemical reactions on the surface of a nanoparticle result in the Zeta Potential of that nanoparticle . For example, silica nanoparticles are tetrahedral complexes of silicon dioxide molecules. On the surface of the silica particles the...

...to adsorb onto the silica. Such metal ions are therefore closely associated with the silica nanoparticles , not easily removed from such particles.

The nanoparticles useful in this invention will typically have a first Zeta Potential and a second Zeta Potential after adsorption of the metal ion onto the nanoparticle due to the addition of the oppositely-charged metal ions. The Zeta Potential change of the nanoparticle is related to the amount of metal ions adsorbed onto the nanoparticle . This relationship provides a measurement for determining the amount of adsorbed metal ions and a...

...instance, the addition of a dilute solution of copper chloride drop-wise to a silica nanoparticle solution until the Zeta Potential of the silica suspension changed from -25 millivolts to a...

...millivolts, was found to be provide a sufficient concentration of metal ions adsorbed onto the nanoparticles to remove particular odorous compounds. In one embodiment of this invention the nanoparticle has a difference between the first and second Zeta Potential of at least about 1.0 millivolt and suitably at least about 5.0 millivolts.

The modified **nanoparticles** of this invention are modified in one embodiment with metal ions that ionically bond with...

...electric potential. Positively charged metal ions are adsorbed onto a negatively charged surface of a **nanoparticle** and vice versa. Examples of metal ions

8

useful in this invention include, without limitation...

...iron (III) ion (Fe^{3+}) and combinations thereof.

In one embodiment of this invention a modified **nanoparticle** useful in this invention has a negative Zeta Potential and adsorbs positively charged metal ions. One suitable modified **nanoparticle** has a negative Zeta Potential of about -1 to -50 millivolts and suitably about -1 to -20 millivolts. In one embodiment of this invention the modified **nanoparticle** having a negative Zeta Potential is a silica **nanoparticle**. Silica **nanoparticles** useful in this invention are available from Nissan Chemical Industries, Ltd., Houston, Texas, under the name SNOWTEX, and have a particle size range of about 1-100 nanometers. The silica **nanoparticles** can be modified with a positively charged metal ion such as copper ions, silver ions, gold ions, iron ions, and combinations thereof.

In another embodiment of this invention the modified **nanoparticle** useful in this invention has a positive Zeta Potential and adsorbs negatively charged metal ion complexes. One suitable modified **nanoparticle** has a positive first Zeta Potential of about 1 to 70 millivolts and suitably about 10 to 40 millivolts. In one embodiment of this invention the modified **nanoparticle** having a positive Zeta Potential is an alumina **nanoparticle**. Alumina **nanoparticles** are also available from Nissan Chemical Industries, Ltd., Houston, Texas, under the name ALUMINASOL, and...

...AK (Alumina coated silica) and have size ranges of about 1-300 nanometers. The alumina **nanoparticles** can adsorb negatively charged metal complexes such as permanganate (MnO_4^-). In an alternative embodiment of the invention, the modified **nanoparticles** can include metal components that are associated with them, but which association is not entirely...

...Numerous techniques may be utilized to form a stronger bond between the transition metal and **nanoparticles**. Silica sols, for example, are generally considered stable at a pH of greater than about...

...342689978 US and such Application is hereby incorporated by reference in its entirety.

The unmodified **nanoparticles** are merely the previously described **nanoparticle** materials without the addition of metal components along their surfaces. The unmodified **nanoparticles** may have predispositions themselves to the adsorption of particular odors. For instance, in blending such...

...of unmodified alumina particles to adsorb acid-based odors/gases and the predisposition of silica **nanoparticles** to adsorb aldehyde-based odors/gases is desirably considered.

Unmodified **nanoparticles** are further described in described in Attorney Docket Number KCX-665 (19232) filed October 16...

...of this invention. The addition of a metal ion adsorbed onto the surface of a **nanoparticle** , as in this invention, provides an active site for capturing and neutralizing gases and odorous compounds. In addition, the modified **nanoparticles** of this invention still have the large surface area that is useful in absorbing other odorous compounds. The metal component active sites of the modified **nanoparticles** are particularly useful in removing odorous compound such as mercaptans, ammonia, amines, and mono- and...

...and aliphatic terpenoids can be removed by adsorption onto the large surface area of the **nanoparticles** . Modified **nanoparticles** are useful in removing odors caused by sulfides, disulfides, trisulfides, thiols, mercaptans, ammonia, amines, isovaleric...

...acid, propionic acid, hexanal, heptanal, 2-butanone, 2-pentanone, 4-heptanone, and combinations thereof. Modified **nanoparticles** can also remove gases such as ethylene gas, carvone, dienals, and terpenoids.

More than one type of metal ion can be coated onto a single **nanoparticle** or multiple **nanoparticles** . This has an advantage in that certain metal ions may be better at removing specific gases and/or odorous compounds than other metal ions even on individual **nanoparticles** . In one embodiment of this invention, more than one type of metal ion are adsorbed onto different **nanoparticles** that are then blended together, for removing at least two gaseous compounds or odorous compounds from an environment.. In this fashion, modified **nanoparticles** of this invention can be used in combination with other modified **nanoparticles** for efficient (or targeted) removal of various gases and odors.

For instance, In one embodiment of this invention copper ion modified silica **nanoparticles** are used in combination with permanganate ion modified magnesium oxide **nanoparticles** . By using the two different modified **nanoparticles** in combination, numerous odorous compounds can be removed. For example, the modified silica **nanoparticle** is useful for removing sulphur and amine odors and the modified magnesium oxide **nanoparticle** is useful in removing carboxylic acid odors. Combining modified **nanoparticles** of this invention therefore allows for removal of a broader range of odors.

In a second embodiment, the modified **nanoparticles** as previously described, may be combined with the unmodified **nanoparticles** for a broad range of adsorption options.

For instance, in one embodiment, at least one type of modified **nanoparticle** is blended with at least one type of unmodified **nanoparticle** . In still another alternative embodiment, at least two types of modified **nanoparticles** are blended with at least one type of unmodified **nanoparticle** .

Typically, the **nanoparticles** described are in either colloidal form or suspensions.

"Colloidal" **nanoparticles** refer to **nanoparticles** that may exist as a stable liquid dispersion.

The **nanoparticles** of the present invention may possess various forms, shapes, and sizes depending upon the desired result. For instance, the **nanoparticles** may be in the shape of a sphere, crystal, rod, disk, tube, string, etc. The average size of the **nanoparticles** is generally less than about 100 nanometers, in some embodiments from about 1 to about...

...size of a particle refers to its average length, width, height, and/or

diameter.

The nanoparticles may have a surface area of from about 50 square meters per gram (m²/g...Society, Vol. 60, 1938, p. 309, with nitrogen as the adsorption gas. In addition, the nanoparticles may also be relatively nonporous or solid. That is, the nanoparticles may have a pore volume that is less than about 0.5 milliliters per gram...

...0.3 ml/g. Without intending to be limited by theory, it is believed that nanoparticles having such a small size and high surface area may improve the adsorption capability of the nanoparticles for many odorous compounds. Moreover, it is believed that

12

the solid nature, i.e., low pore volume, of the nanoparticles may enhance the uniformity and stability of the nanoparticles, without sacrificing its odor adsorption characteristics.

As previously stated, the nanoparticles may be formed from a variety of materials, including, but not limited to, silica, alumina...

...zinc oxide, copper oxide, organic compounds such as polystyrene, and combinations thereof. For example, alumina nanoparticles may be used for odor reduction in accordance with the present invention. Some suitable alumina nanoparticles are described in U.S. Patent No. 5,407,600 to Ando, et al., which...

...in its entirety by reference thereto for all purposes. Further, examples of commercially available alumina nanoparticles include, for instance, ALUMINASOL 100, ALUMINASOL 200, and ALUMINASOL 520, which are available from Nissan Chemical Industries Ltd.

Alternatively, silica nanoparticles may be utilized, such as SNOWTEX-C, SNOWTEX-0, SNOWTEX-PS, and SNOWTEX-OXS, which...

...alumina-coated silica particles may be used, such as SNOWTEXAK available from Nissan Chemical.

The nanoparticles, such as referenced above, may possess units that may or may not be joined together...

...units are joined generally depends on the conditions of polymerization. For instance, when forming silica nanoparticles, the acidification of a silicate solution may yield Si(OH)₄. If the pH of...

...units may tend to separate and gradually grow to form a "silica sol." Such silica nanoparticles may generally be formed according to any of a variety of techniques well known in...

...in their entirety by reference thereto for all purposes.

In one particular embodiment, a silica nanoparticle sol is formed using an ionexchange technique. For exemplary purposes only, one such ion-exchange...

...nanometers, and that is substantially free from any polyvalent metal oxides, other than silica.

Modified nanoparticles are made from unmodified nanoparticles by several

methodologies. In one desirable method, they are made by mixing unmodified nanoparficles with...

...metal ions in the solution.

The metal ions are drawn to and adsorbed onto the **nanoparticles** due to the electric

14

potential differences. The Zeta Potential of a **nanoparticle** changes after the adsorption of metal ions according to this invention. Thus the Zeta Potential can be used to monitor the adsorption of metal ions onto the **nanoparticle**. The formation of such modified **nanoparticles** is described in detail in US Patent Serial Number 101137052 entitled Metal Ion Modified High...

...tools, for effective odor removal and control. Unlike activated charcoal deodorants, the unmodified and modified **nanoparticle** blends of this invention maintain their odor neutralizing effects in solution. It should be recognized that use of the phrase unmodified and modified **nanoparticle** blend is meant to encompass either blends of modified and unmodified high surface area materials...

...of different unmodified high surface area materials or combinations of each. The unmodified and modified **nanoparticle** blends of this invention also maintain odor neutralizing properties when dry and in aerosol form ...

...allows for uses in various commercial product applications. Other advantages of the unmodified and modified **nanoparticle** blends are that they are colorless in solution and white in powder form (activated charcoal is typically black).

As previously stated, the unmodified and modified **nanoparticle** blends can be used to reduce/eliminate headspace odor from product packaging. For instance, the unmodified and modified **nanoparticle** blends of this invention can be applied to various materials for insertion into product packaging. In one embodiment of this invention the unmodified and modified **nanoparticle** blends are held onto a surface of a material for insert, by the electrical potential differences between the unmodified and modified **nanoparticle** blends (Zeta Potential) and the material surface (Streaming Potential).

As an example, the unmodified and modified **nanoparticle** blends of this invention can be applied as a solution to a surface and dried...

...absorbs gas and/or odors. In one embodiment of this invention "the unmodified and modified **nanoparticle** blends are coated onto inserts to be placed inside product packaging. Such inserts may be...

...nature of the product that is contained within the product packaging.

The amount of the **nanoparticles** present on the insert may vary depending on the nature of the insert and its...

...and then multiplying by 100. Higher add-on levels may provide optimum odor reduction.

The **nanoparticles** may be applied to an insert using any of a variety of well-known application...

...insert include printing, dipping, spraying, melt extruding, solvent coating, powder coating, and so forth. The **nanoparticles** may be incorporated within the matrix of the insert and/or applied to the surface thereof. For example, in one embodiment, the **nanoparticles** are

coated onto one or more surfaces of the insert. When coated onto the insert...

...in some embodiments, from about 4 to about 200 nanometers.

The percent coverage of the **nanoparticles** on the surface of the insert may be selected to achieve the desired odor reduction...

...placed (such as adhesively applied) on the inside surface of a product packaging. Alternatively, the **nanoparticle** blend may be coated onto a portion of the inside surface of the product packaging...

...not in contact with the product. In still another alternative embodiment of this invention, the **nanoparticle** blend may be placed/coated on a portion of a product itself to be contained...

...the outer tissue layer (s) of the product. However, it is desirable that if the **nanoparticle** blend is placed on a product itself, it is placed in such a location that it does not impact a consumer's ultimate use of the product.

Unmodified and modified **nanoparticle** blends can be coated in various amounts depending on need. Suitably, unmodified and modified **nanoparticle** blends are coated on fabrics, films, or fibers in an amount of about 0.001...

...and more suitably about 0.1 grams per square meter.

In a desirable embodiment, a **nanoparticle** blend is directly associated with a tissue product by being applied to the paper rolls...

...45 including a hollow, cylindrical cardboard core 50, a blend of different metal modified silica **nanoparticles** have been applied as a coating to the inside surface of the roll core 50. Such **nanoparticles** may be applied prior to bathroom tissue packaging (during manufacture), such as while the core...

...the headspace 60 between the rolls 45 and packaging 55, can be adsorbed by the **nanoparticle** blends of the inventive composition. As can be seen in Fig.

3, the blends of **nanoparticles** can be positioned on a disc insert 51 contained in the package, on an inside...

...a portion of the product 50, contained within the package.

In an alternate embodiment, the **nanoparticle** blends can be added to the core, insert or packaging in conjunction with additional chemistries...

...chemical agent may be added to the core, insert or packaging along with such blended **nanoparticles** .

It should therefore be recognized that methods for removing odor from a product packaging (and...

...or a portion of the product contained within the product packaging.

The unmodified and modified **nanoparticle** blends are exemplified by the following demonstrated **nanoparticle** /odor affinities and the following product example.

Each of the formulated **nanoparticle** types can be blended in either dry or wet form following formation, prior to blend...

...The blends may be accomplished by mixing water suspensions of at least two different modified **nanoparticles** with stirring, or alternatively mixing water suspensions of modified **nanoparticles** with unmodified **nanoparticles**. The mixtures can then be applied to a desired substrate. Alternatively, the desired substrate can be treated/coated with a first **nanoparticle** suspension and then treated/coated with a second **nanoparticle** suspension. While the examples are meant to further describe the inventive compositions and product configurations, they are not meant to be limiting.

Nanoparticle Affinities

In evaluating the affinities of unmodified and modified **nanoparticles** for adsorbing particular odors/gases, testing was conducted on the **nanoparticles** and odors/gases in question. Testing was in accordance with the following procedure.

Test Methods...

...of the chemical odor component of the control package (no treatment) to that of the **nanoparticle** treated package. Thus % odor reduction was expressed in this manner.

The data suggests that for optimal odor removal, **nanoparticles** with the proper metal modification should first be determined, or alternatively, the proper unmodified **nanoparticles** should be identified. In such a fashion, a blend of appropriate odor reducing **nanoparticles** may be compiled in accordance with specific product needs. The blending technology offers the versatility...

...that the human nose can detect). By determining this information one can then design the **nanoparticle** blend that would remove all the chemical components of the odor most efficiently.

An examples...

...19 1.2 87.3

Trimethyl 0.33 0.03 ----- 7.3

Amine

The designed **nanoparticle** blend for the cat odor would comprise metal modified **nanoparticles** (amine odor removal) as the major component with the minor amount being the unmodified alumina **nanoparticle** (for acid removal). This ratio is due to the amines giving rise to over 98...

...is higher. One would only require a small amount (100 times less) of the alumina **nanoparticles** in the blend in order to remove the low concentration (2.4ppb) of the acid odor.

In the second example one can design a very specific odor absorbing **nanoparticle** blend that would work on removing sock odor.

21

Sock odor can be broken down...

...3 11.3

Hydrogen 0.41 0.7 8.1 6.4

Sulfide

The specific **nanoparticle** blend would be a mixture of alumina and metal modified silica **nanoparticles**. The alumina **nanoparticles** would be in

twice the concentration compared to the metal modified silica nanoparticles of the blend. There is twice the acid odor in the "sock odor" as there is sulfide odor.

UNMODIFIED NANOPARTICLE AFFINITY FOR ODOR ADSORPTION EXAMPLE 1

The effectiveness of the unmodified nanoparticles to adsorb odorous compounds was demonstrated. Three types of silica nanoparticles were tested. Specifically, the silica nanoparticles were SNOWTEX-PS, SNOWTEX-O, and SNOWTEX-C, all of which are commercially available from...

...dry on the sash of a fume hood. After drying, the add-on level on nanoparticle solids was approximately 2.4% wt/wt based upon the weight of the tissue.

The...

...removed / g causing
sample) chemical
removed
SNOWTEX-C 90 22

As indicated, the unmodified silica nanoparticles were capable of effectively adsorbing aldehyde and ketone odors when contained on a fibrous substrate.

UNMODIFIED NANOPARTICLE AFFINITY FOR ODOR ADSORPTION EXAMPLE 2

The effectiveness of the unmodified nanoparticles to adsorb other malodorous compounds was demonstrated. Two types of nanoparticles were tested. Specifically, the nanoparticles were SNOWTEX-C and SNOWTEX-AK, all of which are commercially available from Nissan Chemical...

...were present at approximately 20 wt.% solids in the solution.

10 milliliters of the silica nanoparticles were dried at 800C to form powders that were then ground to a surface area...

...sample) removed
SNOWTEX-C 105 78
SNOWTEX-AK 84 68

As indicated, the unmodified silica nanoparticles were capable of effectively adsorbing the pyridine odor when contained on a substrate.

24

MODIFIED NANOPARTICLE AFFINITY FOR ODOR ADSORPTION EXAMPLE 3

A dilute suspension of modified silica nanoparticles was made by adding 1 milliliter of SNOWTEX C, available from Nissan Chemical Industries, Ltd ...

...Potential between the solutions was evidence that the metal ions had adsorbed onto the silica nanoparticle .

A furfuryl mercaptan solution was prepared for testing the odor removal properties of the modified silica nanoparticles . A stock solution of 0.001 percent by weight furfural mercaptan solution, available from Aldrich...

...was greatly reduced, and the detectable odor as well, with the addition of the modified nanoparticles .

25

MODIFIED NANOPARTICLE AFFINITY FOR ODOR ADSORPTION

EXAMPLE 4

The SNOWTEX C/copper ion suspension was tested on...

...9 summarizes the comparison of the HPLC peaks for the 4 samples. The modified silica **nanoparticles** performed substantially better in removing the urine components than other materials.

Table 9-Urine component...

...Maus Maus Maus

Urine + Modified 0 0 12 0 701 2 Maus

Silica Maus Maus

Nanoparticles

Urine + Purite 773 300 0 17 820 156

Latex Particles Maus Maus Maus Maus Maus...

...Activated 900 0 50 17 820 10

Charcoal Maus Maus Maus Maus Maus

26

MODIFIED **NANOPARTICLE** AFFINITY FOR ODOR ADSORPTION

EXAMPLE 5

The odor removal properties of a modified **nanoparticle** when dry and coated on a surface was tested by coating a 10.16 centimeter...

...the untreated paper towel. However, no odors penetrated the paper towel treated with the modified **nanoparticles** for about three hours. After three hours the modified **nanoparticles** were saturated and the odors were detectable. The treated paper towel developed a dark area over the beaker during testing resulting from the binding of the furfuryl mercaptans.

MODIFIED **NANOPARTICLE** AFFINITY FOR ODOR ADSORPTION

EXAMPLE6

The odor removing properties of modified **nanoparticles** as an invisible ...standard bathroom tile (15 centimeter x 15 centimeter) from Home Depot with copper modified silica **nanoparticles** of Example 3. The suspension of copper modified silica **nanoparticles** was applied to a KIMWIPES@ wiper.

The moist KIMWIPES@) wiper was used to wipe the...

...desiccator, once with an untreated control tile in the desiccator, and once with the modified **nanoparticle** treated tile in the desiccator. The ammonia gas was measured by use of a Drager...

...tile and with the untreated tile. The ammonia concentration in the desiccator with the modified **nanoparticle** treated tile was measured at less than 2 parts per million. The modified **nanoparticles** on the standard bathroom tile were effective in substantially reducing ammonia gas and odor.

MODIFIED **NANOPARTICLE** AFFINITY FOR ODOR ADSORPTION

EXAMPLE7

To demonstrate the odor removing properties of modified organic **nanoparticles** of this invention copper ions were adsorbed onto polystyrene **nanoparticles**. A dilute suspension of modified polystyrene **nanoparticles** was made by adding 1.0 milliliter of polystyrene **nanoparticle** suspension, the **nanoparticles** having a particle diameter of 64 nanometers, available from Polysciences, Inc., Warrington, Pennsylvania, to 9.0 milliliters of deionized water. The polystyrene **nanoparticle** suspension had a Zeta Potential of -49 millivolts, as

measured by the Zetapals Unit as...

...of 0.01 percent by weight copper chloride (CUC12) solution was added to the polystyrene nanoparticle suspension. After the addition of the 2 drops of copper chloride solution the Zeta Potential...

...polystyrene solution was measured at -16 millivolts, thus confirming copper ion adsorption onto the polystyrene nanoparticles. One drop of the modified nanoparticle solution was added to a 2.0 milliliters of 0.001 percent by weight solution...

...Example 3 was used to measure furfuryl mercaptan presence before and after adding the modified nanoparticles. The area of the furfuryl mercaptan peak before the addition of the modified nanoparticles was 193 milliabsorption units and after the addition of the modified nanoparticles was 14 milliabsorption units. The copper modified polystyrene nanoparticles proved useful in removing sulphurous compounds.

MODIFIED NANOPARTICLE AFFINITY FOR ODOR ADSORPTION

EXAMPLE 8

A dilute suspension of modified silica nanoparticles was made by adding 1 milliliter of SNOWTEX C, available from Nissan Chemical Industries, Ltd

...C/iron (111) chloride suspension at +13 millivolts. One drop of each of the modified nanoparticle solutions was added to a separate 2.0 milliliter solution of 0.001 percent by...

...3 was used to measure furfuryl mercaptan presence before and after adding the different modified nanoparticles. The results are summarized in Table 10. Each of the modified nanoparticles were successful in removing furfural mercaptan from the solution. Additionally, iron (111) ion modified silica nanoparticles had a positive Zeta Potential which can allow application to fabrics made from materials such...

...97%

In the following Table 11, the adsorption of ammonia by various metal modified nanoparticles was comparatively evaluated. In particular, the analysis of dried modified nanoparticles confirmed that the nanoparticles are effective in removing triethylamine (TEA) odors. In conducting the review, a small amount of metal modified nanoparticle suspension was placed in a vial and allowed to air-dry at ambient conditions. A...

...data that the TEA is efficiently removed by both the Copper and Iron III modified nanoparticles, while unmodified nanoparticles do a much less efficient job of TEA removal. For other chemistries, as illustrated in...

...the odors caused by other chemistries. For instance, ammonia adsorption experiments with metal modified silica nanoparticles demonstrated a high capacity of the modified nanoparticles for ammonia gas. Experiments with 1000 ppm ammonia did saturate the nanoparticles as can be seen in Table 12 below.

30

Table 12

Sample	Ammonia Gas Detected (ppm)	% Removed
--------	----------------------------	-----------

Control	1000	0
---------	------	---

Iron (111) Silica	220	78
-------------------	-----	----

Copper/Silica 210 80
Silver...

...30

KIMWIPES@ Control 900 10

It can be observed from the data that zinc modified **nanoparticles** have little ability to remove ammonia gas, while silver modified **nanoparticles** ; have a very strong ability to remove ammonia gas.

The data in Table 13 below indicates a situation in which unmodified silica **nanoparticles** were optimal for removal of a specific chemical odor. For this study Silica, Silica/Copper and Silica/(ron (111) **nanoparticle** coated KIMWIPES@ were analyzed for their ability to remove ketone and aldehyde odors. The results demonstrate that unmodified silica **nanoparticles** perform better for ketone odor removal than do copper or iron(III) modified silica **nanoparticles** . Specifically, the samples were tested for removal of 2,3Butanedione.

Table 13
Sample % Removed Mg...

...01g) 18.85 99

Silica/Iron (111) (0.01g) 17.33 82

Similarly, unmodified silica **nanoparticles** performed better for odor removal in removing aldehyde odors (3-methyl-butanal) as can be...

...01g) 1.6 0 (approximately)

Silica/iron (111) (0.01g) 0.99 0 (approximately)

MODIFIED **NANOPARTICLE** AFFINITY FOR ODOR ADSORPTION

EXAMPLE9

This example illustrates the method of preparing a copper ion coating on a

nanoparticle that has a high surface area (508m²/g)

The potential to deposit copper hydroxide as an insoluble layer onto silica **nanoparticles** was successfully demonstrated. SNOWTEX-OXS (Nissan Chemical America, Houston, TX) a commercial 10% wt/wt suspension of 4-6nm diameter **nanoparticles** was adjusted to pH 8.7 and a solution of copper chloride added with high...

...charged. The copper hydroxide coated silica sample retains the high surface area of the silica **nanoparticle** starting material.

In practicing blends of the current invention, it may be desirable, depending upon...

...described in the following examples, may be used to create such a coated insert.

MODIFIED **NANOPARTICLE** AS PART OF DURABLE COATING EXAMPLE 10

Base sheet preparation: A dilute suspension of modified silica **nanoparticles** was made by adding SNOWTEX-AK **nanoparticles** from Nissan Chemical Industries to deionized water to produce a 2 weight percent solution. A...

...an amount of 120 milliliters was added to 1120 ml of the 2 weight percent **nanoparticle** solution. Approximately 28.75 grams of Acid Blue 45, also from Aldrich Chemical Company was...

...7 microns 35230 4813

0.5 microns 57841 8557

0.3 microns 78019 13362

MODIFIED NANOPARTICLE AS PART OF DURABLE COATING

EXAMPLE11

A dilute suspension of modified silica nanoparticles was made by adding SNOWTEX-O nanoparticles from Nissan Chemical Industries to deionized water to produce a 2 weight percent solution. A...

...0.5 ml amount of the PEI solution was added to 300 ml of the nanoparticle solution with the further addition Of CUC12 (Aldrich Chemical Company) in a sufficient amount to...

...of the fan blowing. The sample with PEI lost no silicon, indicating that the silica nanoparticles were

34

well bonded to the towel. The odor removal capability was also tested and ...

...Application Example

In order to demonstrate the efficacy of including a blend of odor reducing nanoparticles within a product packaging, a small gauge hypodermic syringe was used to inject 1 ml of iron modified nanoparticle silica (20 % active) into a cardboard roll core of a KLEENEX@ COTTONELLE@ Aloe and E...

...The same method of injection was used to add both unmodified and iron modified silica nanoparticles to KLEENEX @COTTONELLE@ Aloe and E 4 pack bathroom tissue.

While the invention has been...

Claim

... method of claim 1 wherein the differently modified high surface area materials comprise metal modified nanoparticles .

4 The method of claim 1 wherein the step of applying is comprised of applying...

...claim 6 wherein the modified and unmodified high surface area materials comprise unmodified and modified nanoparticles .

36

. The method of claim 6 wherein the step of applying is comprised of applying...

...product within an enclosure formed by the packaging material; and a blend of differently modified nanoparticles contained within said packaging material enclosure; whereby as odor or gas is generated within said...

...within an enclosure formed by the packaging material; and a blend of modified and unmodified nanoparticles contained within said packaging material enclosure; whereby as odor or gas is generated within said...

4/3,KWIC/24 (Item 7 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01233619 **Image available**

VISUAL INDICATING DEVICE FOR BAD BREATH

DISPOSITIF D'INDICATION VISUELLE DE MAUVAISE HALEINE

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Detailed Description

Claims

Detailed Description

... the like.

Brief Description of the Drawings

Figure 1 shows a standard curve for the detection of furfuryl mercaptan
by Michler's
Hydrol-dye;

Figure .2 shows a standard curve for the detection of ammonia by
MH-dye;

Figure 3 shows simple breath testing devices according to one embodiment
of...

...of the Invention

The invention provides simple visual breath testing devices which are
able to detect levels of sulfur and/or ammonia compounds in a user's
breath which are indicative of bad breath. Thus, the breath...

...to 0.5% wt/wt.

The substrate, typically a cellulose tissue, may be coated with **nanoparticles** to provide a high surface area coating on the substrate, i.e., higher than the...
...cellulose tissue may be given a boost in surface area by coating it with the **nanoparticles**. The treated substrate may be then coated with the visual indicating dye.

It's believed...

...thinner coating and thus improving the sensitivity of the device.

The average size of the **nanoparticles** is generally less than about 100 nanometers, in fact it may be from about...

...size of a particle refers to its average length, width, height, and/or diameter.

The **nanoparticles** may have a surface area of from about 50 square meters per gram (m²/g)...

...some cases, from about 180 m²/g to about 240 M²/g.

In addition, the **nanoparticles** may also be relatively nonporous or solid. That is, the **nanoparticles** may have a pore volume that is less than about 0.5 milliliters per gram...

...g. It is believed that the solid nature, i.e., low pore volume, of the **nanoparticles** may enhance the uniformity and stability of the **nanoparticles**.

Examples of commercially available alumina **nanoparticles** include, for instance, Aluminasol@ 100, Aluminasol@ 200 and Aluminasol@ 520, which are available from Nissan Chemical America Corporation, Houston, TX, USA. Alternatively, silica **nanoparticles** may be utilized, such as Snowtex-C@, Snowtex-00, Snowtex-PSO and Snowtex-OXS@ **nanoparticles**, which are also available from Nissan Chemical.

Snowtex-OXS@ **nanoparticles**, for instance, have a particle size of from 4 to 6 nanometers, and may be...

...meters per gram. Also, alumina-coated silica particles may be used, such as Snowtex-AK@ **nanoparticles** available from Nissan Chemical.

The breath testing device includes a simple supporting member, such as...

...KIMWIPES@ tissues from Kimberly-Clark Corporation of Dallas, TX, USA were coated with Snowtex-O@ **nanoparticles** (pH 4.1), available from Nissan Chemical, and were used in the examples described herein...

...1 mg/ml stock solution of MH-dye 16 was applied on a Snowtex7lm-0 **nanoparticle**-coated Scoff@ paper towel and allowed to air dry. The dye-coated paper towel was...

...the electronic devices.

14

Example 9

KIMWIPES@ tissues were coated with a 5% Snowtex-O@ **nanoparticle** solution

from Nissan Chemical and then air-dried. 5.0 mg/ml stock solution of MH-dye in acetonitrile was applied to the Snowtex-O@ **nanoparticle**

-coated KIMWIPESO tissues and a blue color was observed to develop as the applied dye...

...Oakland, California, was placed on a cardboard strip 22, and a piece of the dye-@ nanoparticle coated tissue 24 was placed over a first end 25 of the straw 20. Thus...Accordingly, 1 mg/ml stock solution of MH-dye was applied on a Snowtex@-O nanoparticle -coated Scott@ paper towel and allowed to air dry, before being attached to the strip...

Claim

... 4,4'-bis(dimethylamino)-benzhydrol.

6 The breath testing device of claim 4, further comprising nanoparticles

7 The breath testing device of claim 1, comprising a dried residue of an applied...

4/3,KWIC/25 (Item 8 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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01233618 **Image available**

ODOR CONTROLLING ARTICLE INCLUDING A VISUAL INDICATING DEVICE FOR MONITORING ODOR ABSORPTION

ARTICLE POUR COMBATTRE LES ODEURS COMPRENANT UN DISPOSITIF D'INDICATION VISUELLE INDIQUANT L'ABSORPTION DES ODEURS

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW (EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

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Detailed Description
Claims

Detailed Description

... substance, compound, chemical, mixture or absorbent (such as activated carbon, clay, zeolites, coated or rmodified **nanoparticle** silica or alumuina and molecular sieves) useful in controlling odors.

As used herein the term...

...silicates, starches, ion exchange resins, cyclodextrins, molecular sieves or high surface area materials such as **nanoparticles** (see, for example, EP-A-348 978, EP-A510619, WO 91/12029, WO 91/11977...

...and so forth.

Description of the Figures

Figure 1 shows a standard curve for the **detection** of furfuryl mercaptan by 4,4'

bis(dimethylamino)-benzhydrol (BDMB);

Figure 2 shows a standard curve for the **detection** of **ammonia** by BDMB;

Figure 3 shows a standard curve for the **detection** of urea by BDMB;

4

Figures 4(a) and 4(b) show two possible designs...

...ppb), more preferably from > 1 0 ppb, and most preferably >I 00 ppb) of amines, **ammonia**, sulfur compounds, carboxylic acids and aldehydes were identified (Table 3). While the indicating agent may not **detect** the lower levels of odorous compounds immediately, it may change color in response to these...

...BDMB)

Although the odor absorbing agents which are specifically mentioned in the examples below are **nanoparticles** from Nissan Chemical America Corporation of Houston, Texas and Michler's Hydrol from Aldrich Chemical ...

...molecular sieves, which are known in the art, and other high surface area materials or **nanoparticles** may also be used as the odor absorbing agent.

The **nanoparticles** used in the practice of this invention can act as carriers for at least one metal ion present on the surface of the **nanoparticle**, and the metal ion creates an active site that binds with at least one gaseous compound and/or odorous compound thereby removing the compound from the surrounding environment. **Nanoparticles** can also absorb certain gaseous compounds and/or odorous compounds from the surrounding environment by adsorption directly onto the surface of the **nanoparticles**.

The **nanoparticles** are modified with metal ions that ionically bond with cc)mpounds such as gases and...

...on the periodic table. Other ions can be used in the invention as well. The **nanoparticle** may be made from any of silica, alumina, magnesium

oxide, titanium dioxide, iron oxide, gold...

...ion, gold ion, permanganate ion, chlorite ion, persulfate ion, iron ion, and combinations thereof.

Modified **nanoparticles** are made by mixing **nanoparticles** with solutions containing metal ions. Such solutions are generally made by dissolving metallic compounds into...

...metal ions in the solution. The metal ions are drawn to and adsorbed onto the **nanoparticles** due to the electric potential differences.

Further discussion of the modification of **nanoparticles** may be found in US patent application 10/137052, filed on April 30, 2002, which...

...systems known in the art.

The use of pH control in the modification of silica **nanoparticles** was demonstrated using a 10 weight percent suspension of SNOWTEX-OXS@ **nanoparticles** from Nissan Chemical, having an unmodified particle size of 4 to 6 nm. The pH...

...Zeta potential was obtained the addition of copper chloride was stopped. The resulting copper modified **nanoparticle** had a particle size of about 43 nm and a surface area of about 500...

...and air-dry method. The odor absorbing agents for this example were alumina-coated silica **nanoparticles** SNOWTEXAKO, available from Nissan Chemical.

A visual indicating agent, phenol red (also available from Aldrich...

...shown in Figure 2, a standard curve was derived using ammonium hydroxide solution as an **ammonia** odor source detected by BIDMB (MH-dye). In Figure 2 the x-axis is the concentration of **ammonia** in ppb from 0 to 400 and the y-axis is the absorbance at 590...

...Technologies of Chantilly, Virginia (Model # MRX). The absorbance readings were plotted against the concentrations of **ammonia** solutions, with the concentrations being represented as parts per billion (ppb). The sensitivity of **ammonia** detection was very high according to the MH1 5 dye method, and it was shown that...components of, among others, urine, feces, dog and cooking odors.

Example 10

SNOWTEX-Co silica **nanoparticles** from Nissan Chemical were modified by placing 20 mg copper chloride in 20 ml of a 20% wt/wt SNOWTEX-CO **nanoparticle** suspension. KIMWIPESO tissues from Kimberly-Clark Corporation were coated with the copper ion modified silica **nanoparticle** suspension and allowed to air dry. These light green colored KIMWIPES@ tissues were placed into...

Claim

... napkin, tampon, panty shield and incontinence pad.

15 An article for controlling odor comprising a **nanoparticle** selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold...

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01229325

CONJUGATION OF PEPTIDES

CONJUGAISON DE PEPTIDES

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

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Fulltext Availability:

Detailed Description

Detailed Description

... polymeric systems well 1 5 known to those skilled in the art,
micelles, liposomes, microspheres, **nanoparticulates** , liquid crystals
and dispersions thereof, L2 phase and dispersions there of, well known to
those...

...useful controlled release system and compositions are hydrogels,
oleaginous gels, liquid crystals, polymeric micelles, microspheres,
nanoparticles ,

Methods to produce controlled release systems useful for compositions of
the current invention include, but...methyl ester (1.77 g, 5.01 mmol) in
MeCN (30 ml) was added aqueous ammonia (50 ml, 25%; 12.5 g NHO. After
stirring at room temperature for 71 h no more starting material could be

detected by TLC. The mixture was concentrated under reduced pressure, and the residue was resuspended in...

4/3,KWIC/27 (Item 10 from file: 349)
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01210541 **Image available**

IMAGING PATHOLOGY

IMAGERIE DE PATHOLOGIES

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
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Detailed Description

Claims

Detailed Description

... or at least about 40 hours. The magnetic resonance imaging moiety can include a magnetic nanoparticle (e.g., a magnetic metal oxide, e.g., a superparamagnetic metal oxide). The metal oxide can be iron oxide.

In certain embodiments, the nanoparticle can be an amino-derivatized crosslinked iron oxide nanoparticle, and can have an average diameter of from about 5 nm to about 100 nm...

...free amino group.

In some embodiments, the magnetic resonance imaging moiety can include a

magnetic nanoparticle , (e.g., magnetic metal oxide, such as superparamagnetic iron oxide). In certain embodiments, the magnetic nanoparticle can be a small paramagnetic iron oxide (SPIO) or an ultra-small paramagnetic iron oxide (USPIO).

In certain embodiments, the magnetic nanoparticle can be a coated, cross-linked iron oxide (e.g., an iron oxide nanoparticle coated with aminated, cross-linked dextran, e.g., (CLIO)). The magnetic metal oxide can also...

...superparamagnetic compounds and magnetite, gamma ferric oxide, or metallic iron. In certain embodiments, the magnetic nanoparticle can have a relatively high relaxivity, i.e., strong effect on water relaxation.

In some embodiments, the magnetic nanoparticle (e.g., including the nanoparticle and a coating, e.g., a dextran coating) can have an average diameter of from...at least about one week). In certain embodiments, probes having one or more iron oxide nanoparticles can be useful for this purpose.

Magnetic nanoparticles (e.g., having an average particle size of from about 5 nm to about 1...

...large to undergo renal elimination and generally too small to be recognized by phagocytes. Such nanoparticles are eventually internalized, predominantly by cells of the reticuloendothelial system, and the superparamagnetic iron dissolves and joins normal iron pools. An exemplary probe of this type is Cy5...

...subsequent

modifications thereof

In some embodiments, precursor magnetic resonance imaging moieties can include coated magnetic nanoparticles (e.g., cross-linked dextran-coated

nanoparticles). The coatings can be further derivatized with one or more nucleophilic (e.g., amino groups) or electrophilic (e.g., activated ester) functional groups.

Carboxy functionalized nanoparticles can be made, for example, according to the method of Gorman (see WO 00/61191...

...salts are mixed together and are then neutralized with ammonium hydroxide. The resulting carboxy functionalized nanoparticles can be used for coupling amino functionalized groups.

Carboxy-functionalized nanoparticles can also be made from polysaccharide coated nanoparticles by reaction with bromo or chloroacetic acid in strong base to attach carboxyl groups. In addition, carboxy-functionalized particles can be made from amino-functionalized nanoparticles by converting amino to carboxy groups by the use of reagents such as succinic anhydride or maleic anhydride.

Nanoparticle size can be controlled by adjusting reaction conditions, for example, by using low temperature during...

...or gel filtration, as described, for example in U.S. Patent No. 5,492,814.

Nanoparticles can also be synthesized according to the method of Molday (Molday, R.S. and D...

...52(3):353-67, and treated with periodate to form aldehyde groups. The aldehyde-containing **nanoparticles** can then be reacted with a diarnine (e.g., ethylene

17

diamine or hexanediarnine), which...

...form a Schiff base, followed by reduction with sodium borohydride or sodium cyanoborohydride.

Dextran-coated **nanoparticles** can be prepared and cross-linked with epichlorohydrin. The addition of ammonia will react with epoxy groups to generate amine groups, see Hogernann, D., et al., Improvement of MR[probes to allow efficient detection of gene expression Bioconjug. Chem. 2000. 11(6):941-6, and Josephson et al., "High-efficiency...
...when functionalized with amine is referred to as amine-CLIO or NH2-CLIO.

Carboxy-functionalized **nanoparticles** can be converted to amino functionalized magnetic particles by the use of water-soluble carbodiimides and...

...Cy5 CLIO as the candidate probe.

Example 1. Synthesis of Cy5 CLIO

The Amino-CLIO **nanoparticle** (see e.g., Josephson, L., High-efficiency intracellular magnetic labeling with novel superparamagnetic-Tat peptide ...

...novel superparamagnetic-Tat peptide conjugates.

Bioconjug Chem, 10: 186-191, 1999; and the concentration of **nanoparticles** obtained by assuming 2064 iron atoms per crystal (see, e.g., Shen, T., et al...

...iron oxide nanocompounds (MION): physicochemical properties. Magn Reson Med, 30 29: 599-604, 1993). The **nanoparticle**, Cy5 CLIO, was 32 m-n using the volume estimation of laser light scattering (Malvern...

...Ab (Jackson Immunoresearch

Laboratories, West Grove, PA). The fluorescence from GFP (tumor), Cy5.5 25

(**nanoparticle**) and the rhodamine (glia cells and macrophages) were obtained by selecting appropriate excitation and emission...

...tumor relative to the surrounding tissue on T2-weighted images (FIG. 1B) is indicative of **nanoparticle** accumulation, which causes reduction in signal intensity with T2 weighted spin echo pulse sequences. Reduction...

...T2 weighted, but not proton density weighted, images is characteristic of monodisperse superparamagnetic iron oxide **nanoparticles** and is not seen with larger magnetic particles or gadolinium chelates (see, e.g., Rogers...

Claim

... 15 The method of claim 1, wherein the magnetic resonance imaging moiety comprises a magnetic **nanoparticle**.

16 The method of claim 15, wherein the magnetic nanoparticle comprises a magnetic metal oxide.

17 The method of claim 16, wherein the magnetic metal...

...wherein the metal oxide is iron oxide.

19 The method of claim 15, wherein the nanoparticle is an aminoderivatized cross-linked iron oxide nanoparticle .

20 The method of claim 15, wherein the nanoparticle has an average diameter of from about 5 nm to about 100 nm.

21 The method of claim 20, wherein the nanoparticle has an average diameter of from about 20 nm to about 80 nm.

22 The method of claim 20, wherein the nanoparticle has an average diameter of from about 40 nm to about 60 nm.

32

23...

...is a human.

44 The method of claim 2, wherein the probe further comprises a nanoparticle .

45 The method of claim 44, wherein the nanoparticle is an iron oxide nanoparticle .

46 A computer readable medium on which is recorded one or more magnetic resonance images...

4/3,KWIC/28 (Item 11 from file: 349)
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01193921 **Image available**

METHOD FOR CREATING A FUNCTIONAL INTERFACE BETWEEN A NANOPARTICLE ,
NANOTUBE OR NANOWIRE, AND A BIOLOGICAL MOLECULE OR SYSTEM

PROCEDE DE CREATION D'UNE INTERFACE FONCTIONNELLE ENTRE UNE NANOPARTICULE
, UN NANOTUBE OU UN NANOCABLE, ET UN SYSTEME OU UNE MOLECULE BIOLOGIQUE

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU
SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
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METHOD FOR CREATING A FUNCTIONAL INTERFACE BETWEEN A NANOPARTICLE ,
NANOTUBE OR NANOWIRE, AND A BIOLOGICAL MOLECULE OR SYSTEM
PROCEDE DE CREATION D'UNE INTERFACE FONCTIONNELLE ENTRE UNE NANOPARTICULE
, UN NANOTUBE OU UN NANOCABLE, ET UN SYSTEME OU UNE MOLECULE BIOLOGIQUE
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Detailed Description

Detailed Description

METHOD FOR CREATING A FUNCTIONAL INTERFACE
BETWEEN A NANOPARTICLE , NANOTUBE OR NANOWIRE,
AND A BIOLOGICAL MOLECULE OR SYSTEM
STATEMENT REGARDING FEDERALLY SPONSORED
RESEARCH OR...

...of the device. Consequently, chem-FET devices having carbon nanotubes have been used for such detection . The carbon nanotubes are usually used as a bridge between the source and the drain. The presence of certain molecules such as oxygen or ammonia can alter the overall conductivity of the carbon nanotube by the donation or acceptance of...

4/3,KWIC/29 (Item 12 from file: 349)
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01103125 **Image available**

CARBON NANOTUBES: HIGH SOLIDS DISPERSIONS AND NEMATIC GELS THEREOF
NANOTUBES DE CARBONE: DISPERSIONS HAUTEMENT SOLIDES ET LEURS GELS
NEMATIQUES

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Detailed Description
Claims

English Abstract

...1), a sensor medium (3) formed on the substrate, the sensor medium
comprising one-dimensional **nanoparticles**, wherein the one-dimensional
nanoparticles essentially consist of a semiconducting A_xB_y
compound, e.g. V_x...

French Abstract

...un milieu de detection (3) forme sur le substrat, lequel milieu de
detection comprend des **nanoparticules** unidimensionnelles qui sont
principalement constituees d'un compose semi-conducteur A_xB_y...

...du detecteur. La selectivite et la sensibilite du detecteur peuvent etre
personnalisees par dopage des **nanoparticules** unidimensionnelles a
l'aide de differents dopants ou par variation de la concentration de
dopant...

Detailed Description

... and Actuators 1993, B 13-14, 420 - 423 report a similar behavior of an
optical **sensor** based on calcein-poly(acrylonitrile) in the case of
ammonia detection. The sensitivity increased when I/ ...to be the
size, which is in the centimeter scale. Metal oxide sensors can also
detect ammonia, with a **detection** limit of about 25 ppm, but they
suffer from their high power consumption and a...a substrate, a sensor

medium formed on the substrate, the sensor medium comprising one-dimensional **nanoparticles**, wherein the one-dimensional **nanoparticles** essentially consist of a semiconducting A_xB_y compound, wherein the semiconducting A_xB_y compound is...metal compounds have different selectivities towards a target analyte. The material of the one-dimensional **nanoparticles** used for assembling the sensor device are therefore selected depending on the analyte to be...0.001 and 0. When using e.g. V₂O₅ as a material of the one-dimensional **nanoparticles** vanadium may be present in the V⁴⁺ as well as in the V⁵⁺ state. In... example by introducing defects, the sensitivity of the sensor may be enhanced.

The one-dimensional **nanoparticles** used as the sensitive medium in the sensor ...a much larger extension in a longitudinal direction than in directions perpendicular thereto. Usually the **nanoparticles** have dimensions in the micrometer scale in a longitudinal direction and in the nanometer scale in both directions perpendicular thereto. Preferably the one-dimensional **nanoparticles** have a length of less than 100 nm, especially preferred less than 15 nm, most...

...less than 5000 nm², especially preferred less than 50 nm². The length of the one-dimensional **nanoparticles** can conveniently be controlled by the reaction time during the synthesis of the one-dimensional **nanoparticles**. The one-dimensional **nanoparticles** have the shape of a fibre and therefore do not easily self-organize to form a close-packed arrangement as for example **nanoparticles** which have a spherical shape. Therefore voids within the sensor medium are increased allowing a sensor device.

The one-dimensional **nanoparticles** are present in the sensor medium as individual particles. It is sufficient to stabilize the sensor medium just by physical interactions and to deposit the one-dimensional **nanoparticles** on a substrate surface. To increase mechanical stability of the sensor medium the one-dimensional **nanoparticles** may be interlinked by e.g. bifunctional ligands or may be embedded in a matrix. The one-dimensional **nanoparticles** used in the sensor device according to the invention are made from a semiconducting material components A and B of the semiconducting A_xB_y compound the one-dimensional **nanoparticles** have different selectivity towards a given analyte compared to the carbon-SWNT based sensors described by J. Kong et al. loc. cit. Methods for obtaining one-dimensional **nanoparticles**, as used in the sensor device according to the invention, are well established. The one-dimensional **nanoparticles** can easily be modified in their composition, e.g. by addition of a dopant, and...costs and also can be miniaturized to form part of integrated circuits.

The one-dimensional **nanoparticles** may be hollow or filled and may e.g. have the form of a nanotube or a nanowire. Filled one-dimensional **nanoparticles** are preferred.

Further the one-dimensional **nanoparticles** may have various shapes of cross sections, e.g. may have a round (circular) or rectangular cross section. The one-dimensional **nanoparticles** may then have the form of a nanowire or a nanobelt. Nanobelts are especially preferred as sensing material. The sensor medium may also comprise bundles of one-dimensional **nanoparticles**.

The synthesis of one-dimensional **nanoparticles** formed of II-VI-semiconductors or III-V-semiconductors is e.g. described by X. Duan ...P, examples for binary II-VI compounds are ZnS, ZnSe, CdS, and CdSe. One

dimensional **nanoparticles** have been prepared from the above-mentioned semiconducting materials in bulk quantities with high purity...

...for examples can be prepared using the laser assisted catalytic growth (LCG) method.

One-dimensional **nanoparticles** of semiconducting metal oxides can be prepared by a method described by Z. W. Pan...

...metal oxides that can be used as a source for the preparation of one-dimensional **nanoparticles** used ...are e.g. Ga₂O₃, SnO₂, In₂O₃, PbO₂, MnO, Fe₂O₃, WO₃, and GeO₂. One-dimensional **nanoparticles** consisting of semiconducting metal sulfides may be prepared from MoS₂, NbS₂, TaS₂, TiS₂, WS₂, W₂Se₃...e.g. Fe₂O₃, Fe₃O₄, In₂O₃, Sb₂O₃, SnO₂, TiO₂ and SiO₂). The synthesis of Si₃N₄- **nanoparticles** has been described by Han, W.; Fan, S.; Lit g.; Hu, Y. Science 1997, 277...

...P.; Levy, P.; Mihailovic, D. Science 2001, 292, 479 - 481 described the synthesis of one-dimensional **nanoparticles** made from GaSe.

One-dimensional **nanoparticles** can be prepared with a wide range of compounds using a porous template, e.g. via the appropriate technique, for example thermal decomposition or etching, leaving the required one-dimensional **nanoparticles**. Details towards the growth of one-dimensional **nanoparticles** are given e.g. in Caruso, R.A.; Schattka, J.H.; Greiner, A. Adv. Mat...or in combination with each other. For example it is possible to use one-dimensional **nanoparticles** made of pure V₂O₅. The physical characteristics of the one-dimensional V₂O₅ may be modified...

...further material, e.g. WO₃ to the one-dimensional V₂O₅-material. Further different one-dimensional **nanoparticles** made of different semiconducting materials may be used within a single sensor medium of the ...

...according to the invention. The sensor medium then contains e.g. a first one-dimensional **nanoparticle** made of a first semiconducting A_xB_y compound and a second one-dimensional **nanoparticle** made of a second semiconducting A_xB_y compound. Preferably the semiconducting one-dimensional **nanoparticles** are made of a vanadium oxide material. Vanadium pentoxide one-dimensional **nanoparticles** are easily obtained by wet-chemistry, in large amounts and as pure material. They can...C. Coulon, S. Regnault and J. Livage, Langmuir, 2000, 16, 5295- 5303.

The one-dimensional **nanoparticles** can be employed as synthesized in an undoped form. To modify and to tune the...

...sensitivity of the sensors according to the invention towards a target analyte the one-dimensional **nanoparticles** may be doped with a dopant. Sensors with appropriate dopants are highly sensitive and allow...which are incorporated in the structure or immobilized at the surface of the one-dimensional **nanoparticle**. This is possible by exchanging protons at the surface of the one-dimensional **nanoparticle**. In case of vanadium oxide most of the vanadium atoms in the one-dimensional vanadium...V oxidation state hydroxy groups may be formed on the surface of the one-dimensional **nanoparticle** by partially hydrolysing the vanadium oxide in water. Such hydroxy groups are acidic and the...the layered structure of the material enabling exchange by a larger cation.

The one-dimensional **nanoparticles** can also be doped by intercalation of neutral molecules between layers of the one-dimensional **nanoparticles** . This implies swelling of the structure inducing a weakening of the interaction forces between different layers of the one-dimensional **nanoparticle** . Such an intercalation of neutral molecules between layers of vanadium pentoxide xerogels is e.g. .

...It is also possible to immobilize molecules or particles on the surface of the onedimensional **nanoparticle** .

Possible dopants that may be used to dope the sensor medium are ions, like Au salt may also be employed. Also possible is to dip the one-dimensional **nanoparticles** into a solution containing the metal which is used as a dopant in solid form. The metal is then oxidized and incorporated into the one-dimensional **nanoparticles** . Such an incorporation of metal ions into vanadium pento-oxide xerogels has been described e. . .

...an ingredient of a cathode material in a coin cell assembly.

Further the one-dimensional **nanoparticles** can be doped with organic molecules. A broad variety of organic molecules may be used. . . and pyrrole derivatives. The organic molecules are adsorbed on the surface of the one-dimensional **nanoparticles** or intercalated between layers of the one-dimensional **nanoparticles** thereby modifying the physical and chemical characteristics of the one-dimensional **nanoparticles** . For example T.

Kuwahara, H. Tagaya and J. Kadokawa, Inorganic Chemistry Communications, 2001, 4, 63. . .

...S.D. Huang, Angewandte Chemie International Edition, 1999, 38, 1751-1754. Furthermore the one-dimensional **nanoparticles** can be doped with conducting polymers. Such inorganic-organic hybrid microstructures are known e.g. . Furthermore also large organic cations can be incorporated into the structure of the one-dimensional **nanoparticles** . Such a material has been described e.g. by M. Inagaki, T. Nakamura and A for doping the one-dimensional **nanoparticles** . An ion complex that can be used as a dopant according to the invention are. . .

...of the invention the sensor medium of the chemical sensor device additionally comprises a second **nanoparticle** material which preferably has an approximately spherical shape. The incorporation of second **nanoparticles** different from the one-dimensional **nanoparticles** into the sensor medium allows the modification of the sensor selectivity and sensor sensitivity. Metal **nanoparticles** can be formed by evaporation of the metal on the one-dimensional **nanoparticles** pre-immobilized on the substrate. Further metal **nanoparticles** stabilized with an organic shell can be prepared e.g. by wet chemical methods. A method for preparing such **nanoparticles** is e.g. described by M. Brust, J. Fink, D. Bethell, D.J.

Schiffrin and. . .

...Chem. Commun., 1995, 1655 - 1656. This technique is applicable to a wide range of metal **nanoparticles** . Examples are Fe, Au, Ag, Pt, Pd, as well as some binary **nanoparticles** , like Fe/ Pt. Such stabilized **nanoparticles** are soluble in common organic solvents. These **nanoparticles** can be immobilized on the one-dimensional **nanoparticles** by simply dipping the substrate pre-coated with the onedimensional

nanoparticles in the corresponding solution of the second **nanoparticle**. A chemical coupling between the one-dimensional **nanoparticles** and the second **nanoparticles** is possible through a bi- or polyfunctional organic linker compound.

Finally, certain metal ion complexes...doping vanadium pentoxide nanobelts with a metal e.g. gold. It can be doped with **nanoparticles** stabilized with an organic shell, or by evaporation of a thin metal layer or with a metal salt that is converted to **nanoparticles** during the doping process.

According to a preferred embodiment the second **nanoparticles** consists of a semiconducting material. As a semiconducting material may be used e.g. II...also be used as a mass sensitive sensor. The sensitive film comprising the one-dimensional **nanoparticles** is then used as a coating on a piezo-electric material to ...luminescence properties may change when the analyte molecules are adsorbed to the semiconducting one-dimensional **nanoparticles**. This change is due to a change of the electronic states of the one-dimensional **nanoparticles** and/or of the close environment of the one-dimensional **nanoparticles**. Furthermore the one-dimensional **nanoparticles** can be combined with appropriate chemicals, e.g. dyes, to induce a change of optical...on top of the sensor film. By the sorption of the analyte to the onedimensional **nanoparticles** the electronic properties of the sensor are ...used as an array for electronic nose purposes.

The small size of the one-dimensional **nanoparticles** allows readily miniaturisation of the devices. The chemical sensor according to ...g. to be used in a sensor array in an IC device.

The one-dimensional **nanoparticles** used in the chemical sensor device according to the invention have a quite high electrical conductivity. This is especially the case when vanadium pentoxide is used as the one-dimensional **nanoparticles**. Vanadium oxide comprises vanadium in the valence +IV and +V state and therefore already provides...intercalated into the structure of the sensing material. Depending on the length of the onedimensional **nanoparticles** also sensor devices comprising a single one-diniensional **nanoparticle** may be prepared. In this case preferably a single one-dimensional **nanoparticle** is bridging the gap between the two electrodes. A single one-dimensional **nanoparticle** is sufficient to obtain a sensor medium but also several **nanoparticles** may be arranged in a more or less parallel arrangement. One-dimensional **nanoparticles** of smaller size than the gap size of the electrode pair may be arranged to form a network.

The one-dimensional **nanoparticles** then form intersections at which the surface areas of neighboured **nanoparticles** are in contact with each other thereby providing a conductive path between the electrodes. The... the following steps.

- a) providing a substrate having a substrate surface;
- b) providing one-dimensional **nanoparticles** essentially consisting of a semiconducting A_xB_y compound, wherein A, ...and y are as defined above;
- c) coating the substrate surface with the one-dimensional **nanoparticles** thereby obtaining a sensor medium;
- d) providing detection means for detecting a change of a physical and/or chemical property of the sensor medium.

The one-dimensional **nanoparticles** can be prepared by known methods. An overview on methods for obtaining one-dimensional vanadium surfactant

during the preparation of the onedimensional **nanoparticles** introduces a high porosity as has been shown for vanadium alkoxide derived gels by S and sensitivity.

The one-dimensional **nanoparticles** can be deposited on the substrate by spin-coating, drop-coating, dip-coating, brush techniques, ink jet printing technique or any other technique.

The one-dimensional **nanoparticles** can be aligned during deposition e.g. to bridge two chemiresistor electrodes. Alignment of one-dimensional **nanoparticles** is preferred when using only few **nanoparticles** to form a sensor medium and allows a high reproducibility of the fabrication process. Alignment of the one-dimensional **nanoparticles** may be achieved by MIMIC (Micro Moulding in Capillaries) technique described by H.J. Muhr ...room temperature and its high sensitivity.

When using vanadium pentoxide nanofibres as a one-dimensional **nanoparticles** the chemical **sensor** device is sensitive to gases, say CO, H₂, NH₃ but also to SO, O₂ or NO, The **sensor** is highly sensitive to **ammonia** and polar organic molecules, like amines or thiols and **detection** below 0,5 ppm is possible. By changing the dopant, it is possible to create...detection of amines. It could be demonstrated by the inventors that it is possible to **detect** amines in low concentrations down to 30 ppb at high humidity. Biogenic amines are often encountered in fermented foodstuff. For example, trimethylamine or **ammonia** is produced during fish decomposition. Therefore volatile amines may be used as indicator of fish...can also be diagnosed by a specific pattern of volatile amines in urine. In addition, **ammonia** is often used in the chemical industry and the **detection** method according to the invention may be used to **detect** leaks.

Humidity has little effect on the response towards carbon monoxide, acetic acid and Ipropanolfig. 2 schematically displays different types for the arrangement of one dimensional **nanoparticles** to bridge a gap between a pair of electrodes; fig. 3 schematically displays a set...humidities.

Fig. 1 schematically shows a chemiresistor, which has a sensor medium comprising one-dimensional **nanoparticles** (nanobelts) as a sensitive material. On a substrate 1 are placed interdigitated electrodes 2. The electrode structures 2 are covered by a sensor flm, which is formed of one-dimensional **nanoparticles** 3. A constant current may be applied to the leads of the electrodes 2 and...be detected by a detector (not shown).

Fig. 2 displays different arrangements of one-dimensional **nanoparticles** 4 between a pair of electrodes 2. In fig. 2a a single one-dimensional **nanoparticle** 4 is bridging the gap between the pair of electrodes 2. For simplicity only one one-dimensional **nanoparticle** is shown on the figure. Several particles can also be employed. In this arrangement, the analyte can modulate the conductivity along the one-dimensional **nanoparticle** by adsorption on its surface and/or by intercalation. The analyte can also influence the...with the particles changing the intrinsic conductivity of the one-dimensional particles. The one-dimensional **nanoparticles** can have a length much smaller than the gap size between a pair of electrodes. The onedimensional **nanoparticles** are then arranged in a random order to form a network of **nanoparticles** 4 between a pair of electrodes 2 as shown in fig. 2b. Like in the...the interparticle contacts. In this arrangement the analyte enhances or reduces the conduction between the **nanoparticles**. The arrangement shown

in fig. 2b is preferred when the analyte interacts with the interparticle contacts. Between individual one-dimensional nanoparticles 4 are formed voids, which provide an easy access of the analyte to the nanoparticle surface even when a sensor medium of a larger thickness is used.

Fig. 3 schematically...were used to prepare sensor 7.

c) Fabrication of sensors.

1 5 The one-dimensional nanoparticles were deposited onto BK7 glass substrates supporting lithographically made interdigitated electrode structures. The electrode structures...sensor (sensor 7)
The fabrication procedure described under (c) was repeated but as one-dimensional nanoparticles were used silver doped vanadium pentoxide nanofibres obtained under (b). Thereby a silver doped V205...displayed in fig. 3. Whereas sensors 1 and 2 have about the same sensitivity to ammonia (in absolute value), sensor 2 has a sensitivity towards CO which is about 5 times larger than for sensor 1. By combining these two sensors it is therefore possible to distinguish NH₃ and CO. Sensor 3 is less sensitive to ammonia than sensors 1 and 2, but is more sensitive to H₂. This makes this sensor more suitable for applications where detection of hydrogen is required.

h) Influence of doping level

Silver doped vanadium pentoxide sensors 1...R_{ini} of + 1. 0 % and + 1. 3, respectively. This demonstrates that the response of the sensor can be modified by varying the doping level.

i) Sensitivity of silver doped vanadium pentoxide sensors toward NH₃

Sensor 7 was exposed to 360 ppb ammonia. The response of the sensor is displayed in fig. 6. The sensor displayed a fast response of AR/R_{ini} - 1.6 % within 120 seconds. This demonstrates that the sensor is sensitive to very low concentrations of ammonia giving a fast response and a short recovery period. At higher ammonia concentrations an increased response of the sensor is obtained as is obvious from the sensitivity isotherm displayed in fig. 7.

k) Sensitivity...

Claim

... a substrate, a sensor medium formed on the substrate, the sensor medium comprising one-dimensional nanoparticles, wherein the one-dimensional nanoparticles essentially consist of a semiconducting A,,By compound, wherein the semiconducting A,,By compound is...0.

7 Chemical sensor device according to one of the preceding claims, wherein the onedimensional nanoparticles are filled.

8 Chemical sensor device according to one of the preceding claims, wherein the onedimensional nanoparticles have a rectangular cross section.

9 Chemical sensor device according to one of the preceding claims, wherein the onedimensional nanoparticles are provided in the form of a bundle.

10 Chemical sensor device according to one of the preceding claims, wherein the onedimensional nanoparticle further comprises a dopant. 11 Chemical ...one of claims 10 to 13, wherein the dopant is intercalated within the one-dimensional nanoparticle and/or is adsorbed on the

surface of the one-dimensional nanoparticle .

15 Chemical sensor device according to one of the preceding claims, wherein the sensor medium additionally comprises second nanoparticles different from the onedimensional nanoparticles .

16 Chemical sensor according to claim 15, wherein the second nanoparticles have an approximately spherical shape.

17 Chemical sensor device according to claim 15 or 16, wherein the second nanoparticle essentially consists of a metal.

18 Chemical sensor device according to one of the preceding...preceding claims, wherein the sensor material comprises at least I individual of said one-dimensional nanoparticles bridging a gap between two electrodes provided on the substrate. 2 1. Chemical sensor device...the following steps:

- a) providing a substrate having a substrate surface;
- b) providing one-dimensional nanoparticles essentially consisting of a 1 5 semiconducting A,,By compound as defined in claim 1;
- c) coating the substrate surface with the one-dimensional nanoparticles thereby obtaining a sensor medium;
- d) providing detection means for detecting a change of a one-dimensional nanoparticles are aligned on the substrate surface.

25 Method according to claim 23 or 24, wherein the one-dimensional nanoparticles are fixed to the substrate surface by a bifunctional ligand which is linked to the substrate surface by a first functional group and to the one-dimensional nanoparticle surface by a second functional group.

26 Method according to one of claims 23 to...

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MAGNETIC- NANOPARTICLE CONJUGATES AND METHODS OF USE

CONJUGUES DE NANOPARTICULES MAGNETIQUES ET PROCEDES D'UTILISATION

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LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
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MAGNETIC- NANOPARTICLE CONJUGATES AND METHODS OF USE

CONJUGUES DE NANOPARTICULES MAGNETIQUES ET PROCEDES D'UTILISATION

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Detailed Description

Claims

English Abstract

The present invention provides novel compositions of binding moiety-**nanoparticle** conjugates, aggregates of these conjugates, and novel methods of using these conjugates, and aggregates. The **nanoparticles** in these conjugates can be magnetic metal oxides, either monodisperse or polydisperse. Binding moieties can...

French Abstract

...trait a de nouvelles compositions de conjugues constitues d'une fraction de liaison et de **nanoparticules**, a des agregats de ces conjugues et a de nouveaux procedes d'utilisation de ces conjugues et agregats. Les **nanoparticules** presentes dans ces conjugues peuvent etre des oxydes metalliques magnetiques, monodisperses ou polydisperses. Les fractions...

Detailed Description

Magnetic- **Nanoparticle** Conjugates and Methods of Use

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit...

...is incorporated herein by reference in its entirety.

TECHNICAL FIELD

This invention relates to magnetic **nanoparticle** conjugates and methods of use.

BACKGROUND

Magnetic particles are widely used reagents for the purification... particle; their effects on water relaxation rate are unspecified and not relevant to their application. **Nanoparticles** do not respond to the weak, magnetic fields of hand held magnets.

Magnetic particles have...from T2.

In another example, WO 01/19405 describes the preparation and uses of magnetic **nanoparticles** with various biomacromolecules attached.

SUMMARY

The present invention provides new magnetic conjugates and methods for their synthesis and use. Each conjugate comprises a magnetic

nanoparticle linked to a binding moiety that specifically binds to a target in a sample, such...and, in some aspects of the invention, at least two populations of the binding moiety- nanoparticle conjugates.

2 Each conjugate in a population has a plurality, e.g., two, three, four, or more, of a single type of binding moiety attached to a nanoparticle . The nanoparticle is composed of a magnetic metal oxide and ... included, they contain functional groups that enable the binding moiety to be attached to the nanoparticle to form the conjugate. The polymer can be a natural polymer, a synthetic polymer, a...

...carboxy, amino, or sulffiydryl groups. In some embodiments, the binding moiety is attached to the nanoparticle through disulfide groups. The metal oxides can also be associated with non-polymer functional groups to form the nanoparticles .

In one aspect of the invention, a population of conjugates (or a mixture of two...contains superparamagnetic iron oxide crystals. The superparamagnetic character of the iron oxide of the nanoparticle makes it a potent enhancer of water relaxation rates, an enhancement ...invention features an aggregate including a plurality of conjugates, wherein each conjugate includes a magnetic nanoparticle linked to a binding moiety that specifically binds to a target molecule, to another binding... specifically bind to a target molecule, wherein each conjugate in the first population comprises a nanoparticle including a magnetic metal oxide (e.g., a superparamagnetic metal oxide) linked to a plurality... site on the target molecule, and wherein each conjugate in the second population comprises a nanoparticle comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind...

...target molecule.

These compositions can include conjugates that further include functional groups that link the nanoparticles to the binding moieties. The functional groups can be amino, carboxy, or sulffiydryl groups. Alternatively, the conjugates can further include a polymer associated with the nanoparticles , and wherein the functional groups are bound to the polymer and to the binding...covalent bond or by a disulfide bond. For example, oligonucleotides can be attached to the nanoparticles by a single covalent bond at the 3' or 5' end of each oligonucleotide. In...R2 relaxivity between about 15 and 100 mM⁻¹ sec In particular embodiments, the nanoparticle is an amino-derivatized cross-linked iron oxide nanoparticle .

In another aspect, the invention features a conjugate including a magnetic nanoparticle linked to a first binding moiety, wherein the first binding moiety includes a cleavage ...target molecule to form an aggregate, wherein each conjugate in the first population includes a nanoparticle that includes a magnetic metal oxide linked to a plurality of ...site on the target molecule, and wherein each conjugate in the second population includes a nanoparticle including a magnetic metal oxide linked to a plurality of second binding moieties that bind...are capable of forming an aggregate, wherein each conjugate in a first population includes a nanoparticle including a magnetic metal oxide linked to a first binding moiety, wherein the first binding...and second populations of oligonucleotide-nanoparticle conjugates, wherein each conjugate in the first population includes a nanoparticle having ... functional groups; and a plurality of first oligonucleotides attached to the functional groups on the nanoparticle ; and wherein each conjugate

in the second population includes a **nanoparticle** having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle**; wherein the - 8 first and second oligonucleotides are each complementary to first and second portions...as a nucleic acid or polypeptide) from a sample by obtaining a conjugate including a **nanoparticle** having a magnetic metal oxide linked by a cleavable bond (e.g., a reducible disulfide...purification of nucleic acids or materials hybridizing to nucleic acids. The conjugates can be oligonucleotide-**nanoparticle** conjugates having a reducible disulfide bond to couple the oligonucleotides to the **nanoparticles**, and as a result reducing agents can separate the oligonucleotides from the **nanoparticles** at a desired time. Materials bound to the oligonucleotide portion of these oligonucleotide **nanoparticle** 10 conjugates, such as double-stranded nucleic acids, can be obtained by the use...nucleic acid in a plurality of samples, by obtaining first and second populations of oligonucleotide-**nanoparticle** conjugates, wherein each conjugate in the first population includes a **nanoparticle** having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the **nanoparticle**, and wherein each conjugate in the second population includes a **nanoparticle** having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle**; wherein the first and second oligonucleotides are each complementary to first and second portions of ...

...in the other populations; preparing a mixture of the first and second populations of oligonucleotide- **nanoparticle** conjugates; obtaining a plurality of fluid samples; contacting a portion of the mixture with each ...the samples to hybridize to the first and second oligonucleotides of both populations of oligonucleotide- **nanoparticle** conjugates; and simultaneously obtaining the relaxation properties of the fluid in each of the plurality...administering to the subject at least one population of conjugates, wherein each conjugate includes a **nanoparticle** having a magnetic metal oxide linked to a binding moiety that specifically binds to the...levels of mRNA in cells using a mixture of populations of superparamagnetic oligonucleotide-'iron oxide **nanoparticle** conjugates and NM imaging. When the conjugates react with a target, e.g., mRNA, the ...

...array format. In yet another embodiment, the invention features a method in which the oligonucleotide- **nanoparticle** conjugates and an MR detector are ...scheme in which alkanethiooligonucleotides were reacted with N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) activated **nanoparticles** to form **nanoparticle** conjugates P1 and P2. P 1 and P2 10 hybridize with complementary oligonucleotides followed by aggregation and magnetic relaxivity changes. Dithiothreitol (DTT) treatment breaks the bond between **nanoparticle** and alkanethiooligonucleotide.

FIGs. 2A to 2D are images of test tubes illustrating the effect of incubating oligonucleotide- **nanoparticle** conjugates with oligonucleotides. From left to right, 2A: P1 and P2; 2B: P1, P2 plus...

...arrows.

FIGs. 3A and 3B are images of gel electrophoresis of a P1/P2/oligonucleotide **nanoparticle** precipitate. FIG. 3A shows a gel run in non-denaturing conditions. Lane 1: No DTT...values of a turbid medium

(INTRALIPIDS) after a complementary oligonucleotide is added to an oligonucleotide nanoparticle conjugate mixture, P1 and P2. DTT was added after 180 minutes.

FIG. 7 is an...with total RNA extracted from various cell lines. FIG 9B is an image of the nanoparticle conjugates with lysed cells from WT or GFP + human glioma lysate two hours following OA is a graph illustrating the incubation of anti-GFP-P1 nanoparticle conjugates with GFP or BSA protein resulting in a significant decrease in T2. FIG. 1 ...or polysaccharide) linked, e.g., covalently or non-covalently, to a magnetic, e.g., superparamagnetic, nanoparticle. The binding moiety causes a specific interaction with a target molecule (or, ...the spin-spin relaxation time (T2) of adjacent water protons in an aqueous solution.

Nanoparticles

Nanoparticles can be monodisperse (a single crystal of a magnetic material, e.g., metal oxide, such as superparamagnetic iron oxide, per nanoparticle) or polydisperse (a plurality of crystals, e.g., 2, 3, or 4, per nanoparticle). The magnetic metal oxide can also comprise cobalt, magnesium, zinc, or mixtures of these metals...

...superparamagnetic compounds and magnetite, gamma ferric oxide, or metallic iron. Important features and elements of nanoparticles that ...can be covalently attached, (iii) a low non-specific binding of interactive moieties to the nanoparticle, and (iv) stability in solution, i.e., the nanoparticles do not precipitate.

- 14 In all embodiments, the nanoparticles are attached (linked) to the binding moieties via functional groups. In some embodiments, the nanoparticles are associated with a polymer that includes the functional groups, and also serves to keep...other, or that are individually entrapped or surrounded by the polymer.

In other embodiments, the nanoparticles are associated with non-polymeric- functional group compositions. Methods are known to synthesize stabilized, functionalized nanoparticles without associated polymers, which are also within the scope of this invention.

Such methods are described, for example, in Halbreich et al., Biochimie, 80 (5-6):379-90, 1998.

The nanoparticles have an overall size of less than about 100 nm. The metal oxides are...e.g., about 5 to 20 nm thick or more. The overall size of the nanoparticles is about 15 to 200 nm, e.g., about 20 to 100 nm, about 40...that the nanoparticles can be prepared, but in all methods, the result must be a nanoparticle with functional groups that can be used to link the nanoparticle to the binding moiety.

For example, oligonucleotide binding moieties can be linked to the metal ...

...a functionalized polymer or to non-polymeric surfacefunctionalized metal oxides. In the latter method, the nanoparticles can be synthesized according to the method of Albrecht et al., Biochimie, 80 (5-6...made using oligonucleotides that have terminal amino, sulfhydryl, or phosphate groups, and superparamagnetic iron oxide nanoparticles bearing amino or carboxy groups on a hydrophilic polymer. There are several methods for synthesizing carboxy and amino derivatized-nanoparticles. Methods for synthesizing functionalized,

coated nanoparticles are discussed in further detail below.

Carboxy functionalized nanoparticles can be made, for example, according to the method of Gonnard (see WO 00/61191...to attach carboxyl groups. In addition, carboxy-functionalized particles can be made from amino-functionalized nanoparticles by converting amino to carboxy groups by the use of reagents such as succinic anhydride or maleic anhydride.

Nanoparticle size can be controlled by adjusting reaction conditions, for ...or gel filtration, as described, for example in U.S. Patent No. 5,492,814.

Nanoparticles can also be synthesized according to the method of Molday (Molday, R. S. and D aldehyde-containing nanoparticles can then be reacted with a diamine (e.g., ethylene diamine or hexanediamine), which will...

...Schiff base, followed by reduction with sodium borohydride or sodium cyanoborohydride.

I 0 Dextran-coated nanoparticles can be made and cross-linked with epichlorohydrin.

The addition of ammonia will react with epoxy groups to generate amine groups, see Hogemann, D., et al., Improvement of MRI probes to allow efficient detection of gene expression Bioconjug. Chem. 2000. 11(6):941-6, and Josephson et al., "High-efficiency...when functionalized with amine is referred to as amine-CLIO or NH₂-CLIO.

Carboxy-functionalized nanoparticles can be converted to amino-functionalized magnetic particles by the use of water-soluble carbodiimides...

...diamines such as ethylene diamine or hexane diamine.

Avidin or streptavidin can be attached to nanoparticles for use with a biotinylated binding moiety, such as an oligonucleotide or polypeptide. See e...

...acinar cells, " Bioconjug.

Chem., 1996, 7(3):311 Similarly, biotin can be attached to a nanoparticle for use with an avidin-labeled binding moiety.

In all of these methods, low molecular weight compounds can be separated from the nanoparticles by ultra-filtration, dialysis, magnetic separation, or other means. The unreacted oligonucleotides can be separated from the oligonucleotide-nanoparticle conjugates, e.g., by magnetic separation or size exclusion chromatography.

17

Binding Moieties

The binding...solution.

Oligonucleotide Binding Moieties

In certain embodiments, the binding moieties are oligonucleotides, attached to the nanoparticles using any one of a variety of ...bond, e.g., at the 3' or 5' end to a functional group on the nanoparticle . The new conjugates are useful in various types of MR applications,

including but not limited...of the new in vitro assay methods uses at least two populations of oligonucleotide magnetic nanoparticles, each with strong effects on water relaxation (see Table 2). As the oligonucleotide-nanoparticle conjugates react with ...the relaxation properties of the solvent, which are altered when the mixture of magnetic oligonucleotide nanoparticles reacts with a target nucleic acid to form aggregates.

A feature of the analytical method of magnetic metal oxide nanoparticles, each with a specific sequence of oligonucleotide, and each with more than one copy of the oligonucleotide attached, e.g., covalently, per nanoparticle. The assay protocol involves preparing a mixture of populations of oligonucleotide-nanoparticle conjugates and reacting the mixture with a target nucleic acid. Alternatively, oligonucleotide-nanoparticle conjugates can be reacted with the target in a sequential fashion. A second feature of...synthesized by methods known in the art, and used in conjunction with an avidin-bound nanoparticle.

Polypeptide Binding Moieties

In certain embodiments, the binding moiety is a polypeptide (i.e., a... Similar bifunctional conjugation reagents, such as SPDP and reacting with the amino group of the nanoparticle and thiol group of the polypeptide, can be used with any thiol bearing binding moiety...low. For example, up to twenty 2 kDa peptides can be attached to a nanoparticle, calculated assuming 2064 iron atoms per nanoparticle. With larger binding moieties like proteins (generally greater than about 30 kDa) the same mass of attached polypeptide results in only approximately 1-4 binding moieties per nanoparticle. Second, polypeptides can be engineered to have uniquely reactive residues, distal from the residues required for biological activity, for attachment to the nanoparticle. The reactive residue can be a cysteine thiol, an N-terminal amino group, a C...or an ectodomain of a cell surface protein. In each case, the resulting binding moiety-nanoparticle is used to measure the presence of analytes in a test media reacting with the...a covalent bond, at one of the two -ends, to a functional group on the nanoparticle. The polysaccharides can be synthetic or natural.

Mono-, di-, tri- and polysaccharides can be used attachment chemistry to the nanoparticle.

A generally useful method of accomplishing linking is to couple avidin to a magnetic nanoparticle and react the avidin-nanoparticle with commercially available biotinylated polysaccharides, to yield polysaccharide-nanoparticle conjugates. For example, sialyl Lewis x based polysaccharides are commercially available as biotinylated reagents and will...chromatography.

Polysaccharides can also be synthesized and are commercially available.

Coupling of Binding Moieties to Nanoparticles to Prepare Conjugates

The conjugates are prepared by linking two or more binding moieties to each magnetic nanoparticle. A general procedure for synthesizing amino-cross linked iron oxide nanoparticle begins with the synthesis of a dextran coated superparamagnetic iron oxide.

There are a variety...or exhaustive ultrafiltration using a membrane with a 10 kDa cutoff.

Coupling of Oligonucleotides to Nanoparticles

The invention provides for preparing oligonucleotides with reactive 3',

5', or both termini. One terminus is attached to the surface of the **nanoparticle**, leaving the other terminus free for attachment to another molecule, e.g., a biotin group...reagents that can be used to couple 10 oligonucleotides to amino- or carboxy-functionalized **nanoparticles**. The general strategy is to provide an oligonucleotide with a unique reactive group on the...

...end are of particular value, and are commercially available. They can be coupled to amino- **nanoparticles** through the use of reagents such as N-succinimidyl 3-(2pyridyldithio)propionate (SPDP) and long chain SPDP (1c-SPDP) that produce a cleavable disulfide bond between the **nanoparticle** and the oligonucleotide. Amino- **nanoparticles** can also be reacted with reagents such as succinimidyl-iodoacetate to produce non-cleavable bonds between the **nanoparticle** and oligonucleotide.

25 Table 1: Functional Groups and Strategies for coupling oligonucleotides to **nanoparticles**

Oligonucleotide Terminal Group	Nanoparticle Functional Group	Coupling Chemistry	Cleavable
Sulfhydryl	Amino	SPDP, 1c-SPDP	Yes (1c, long...)

...Carboxyl CDI No (carbodiimide)
 Phosphate Amino CDI No
 Biotin Avidin Not applicable Not applicable
 Thus, **nanoparticles** can be conjugated to oligonucleotides through a variety of conjugation chemistries. See U.S. Patent...using coupling chemistries as shown, for example, in Table 1.

In other embodiments, populations of **nanoparticle** conjugates can be synthesized by 10 allowing biotinylated oligonucleotides, polypeptides, or polysaccharides, to react with avidin (or streptavidin)-bound **nanoparticles**. Here a non-covalent, but tight, bond between the biotinylated binding moiety, e.g., oligonucleotide, and avidin of the **nanoparticle** attaches the oligonucleotide to the **nanoparticle**. Oligonucleotide- **nanoparticle** conjugate populations prepared in this fashion are analogous to those prepared with covalent chemistries (Table ...the formation of aggregates and changes in T2. In this case, two populations of oligonucleotide- **nanoparticle** conjugates are formed when the avidin-**nanoparticle** is reacted with two biotinylated oligonucleotides. An advantage of...

...that react with a target oligonucleotide are far smaller, and hence react faster, than oligonucleotide- **nanoparticle** conjugates. Biotinylated-oligonucleotides have molecular weights less than 50 kDa, while oligonucleotide- **nanoparticle** conjugates have molecular weights greater than about 1000 kDa (e.g., 1000, 2000, 3500, 5000...
 ...reactive 3', 5', or both termini. One end is linked to the surface of the **nanoparticle**, leaving the other end free for attachment to another molecule, e.g., a biotin group or another tag.

The conjugation of polypeptides to **nanoparticles** can be accomplished by a large number of conjugation chemistries and reagents some of which are also used for attaching oligonucleotides to **nanoparticles**, see Table 1. A preferred general strategy is to use one of the large number of bifunctional agents that can be reacted first with the amino group of the **nanoparticle**, and secondly with the thiol group of the polypeptide (or biomolecule).

Examples of such bifunctional...The bifunctional agent is dissolved in DMSO and reacted in excess with the amino functionalized nanoparticle at pH 8 using a non-amine containing buffer (e.g., borate, phosphate). Unreacted bifunctional...

- ...Tat peptide conjugates, Bioconjugate Chemistry, 10, 186-91; Perez et al. (2002) DNA-based magnetic nanoparticle assembly acts as a magnetic relaxation nanoswitch allowing screening of DNA-cleaving agents, Journal of...
- ...synthesized by allowing a biotinylated antibody or antibody fragment to react with avidin (or streptavidin) nanoparticles. Here a non-covalent, but tight, bond between the biotinylated antibody and avidin of the nanoparticle attaches the antibody to the nanoparticle.

In another embodiment, a natural or synthetic polypeptide is covalently or noncovalently attached to the nanoparticle while the other terminal is biotinylated.

In one aspect of the invention, both ends of the polypeptide are biotinylated and avidin is directly attached to the nanoparticle.

In another embodiment, both termini of the peptide are covalently or non-covalently attached to two nanoparticles.

Coupling of Polysaccharides to Nanoparticles

The invention provides for preparing polysaccharides with reactive ends. One end is attached to the surface of the nanoparticle, leaving the other end free for attachment to another molecule. For example, as described above...

- ...the polysaccharide can be biotinylated on both termini and exposed to avidin linked to a nanoparticle.

28

Characterizing Conjugates

The conjugates can form several conformations, or "states," in solution. The first...contains 2 to about 20 (e.g., 3, 5, 7, 10, 15, or 20) individual nanoparticle conjugates held together by the interaction (e.g., binding) of the binding moiety with a target, or with another binding moiety. The association of the nanoparticles is mediated by the attached biomolecules and not by nanoparticle non-specific attractions. This aggregate is approximately 100-500 nm (e.g., 200, 250 ...mesh. The size of the openings can be controlled by adjusting the size of the nanoparticles and the size of the binding moieties on each conjugate. The small ...cluster, which is, in effect, an aggregate of aggregates. The cluster contains greater than 20 nanoparticles and is greater than 500 nm in size. The cluster is not useful since it typically clumps and falls out of solution.

The nanoparticle conjugates can be used as magnetic nanosensors or magnetic relaxation switches (MRS) in various detection...non-degradable oligonucleotide analogs (e.g., peptide nucleic acid or PNA) may be coupled to nanoparticles and used to image sequences of nucleic acids in vivo.

Non-toxicity is evident from the use of magnetic nanoparticles as the active ingredient of COMBIDEX6, a nanoparticle-based MR contrast agent, which has been judged approvable by the FDA (January 1999). COMBIDEX8 examples described herein consists of monodisperse or polydisperse, fluid-phase nanoparticles containing superparamagnetic

Fe₂O₃/Fe₃O₄ (3-5 run), caged by epichlorohydrin cross-linked dextran, and functionalized...hybridization conditions are established by methods well known in the art. Hybridization of the oligonucleotide- nanoparticle conjugates to the target nucleic acids is typically performed under moderate to high stringency conditions the oligonucleotide- nanoparticle conjugates and those of the target oligonucleotide or nucleic acid being detected. These techniques and...oligonucleotide and the faster one of a mixture of 3' and 5' oligonucleotides.

- 31 The nanoparticles P1 and P2 are potent ...mean + SD, n 6.

The effect of temperature cycling on the hybridization of the oligonucleotide nanoparticle was investigated by measuring changes in T₂ values (FIG. 5). At 80°C, hybridization was...representative T₂ changes were observed. Furthermore, upon addition of DTT, oligonucleotides were cleaved from the nanoparticles and T₂ did not change during further temperature cycling. These results indicate that oligonucleotide hybridization...

...are fully reversible through the use of DTT.

Selectivi

A unique feature of the magnetic nanoparticles is that they are highly stable to temperature fluctuations and to different ionic media. This... binding to target molecules and form aggregates as described further herein.

Uses of Dindina Moiety- Nanoparticle Conjugates

The new conjugates can be used in two broad applications. In one application, the...of important ways. @

First, HYRAS involves the assay of nucleic acids using superparamagnetic iron oxide nanoparticles, and is based on the observation that nucleic acids do not non-specifically adsorb to...which contain a multiplicity of phosphate groups, do not interact nonspecifically with the iron oxide nanoparticles.

Second, to produce the needed aggregation of nanoparticles by a specific target nucleotide, two types of oligonucleotide- nanoparticles are needed, each with a single type of oligonucleotide attached, each reacting with a different...

...target complementary oligonucleotide (see FIG. 1). If two different oligonucleotides were coupled to the sample nanoparticle, the target nucleic acid would hybridize to the oligonucleotides on the same particle and no...4 of U.S. Patent No. 5,164,297. In contrast, in HYRAS, when oligonucleotide- nanoparticles react with a target ...gold based colorimetric assays described in WO 98/04740. In one method using the gold nanoparticles, the color change is determined in solution, which requires a non- ...In the present invention, neither separation nor amplification steps are used. Instead, the presence of nanoparticle aggregate is detected by NM. The invention can be distinguished by the ability to "see...CLIO, as described herein. Alternatively, non-polymer coated iron oxide particles can be used. The nanoparticles are then coupled to specific oligonucleotides as shown, e.g., in FIG. 1. The resulting oligonucleotide- nanoparticle conjugates are then formulated in a physiologically acceptable media (e.g., ...the mRNA of interest and is bound at the 3' or 5' tennini to the nanoparticle. A second conjugate is synthesized ...below.

Here a microtiter plate is prepared where each well contains different combinations of oligonucleotide- nanoparticles, i.e., combinations of

oligonucleotides with different sequences attached to the same magnetic nanoparticle. The sequences of the oligonucleotides are chosen to permit hybridization, followed by aggregation and T2...

...in a sample. In this method, antibodies are linked covalently or non-covalently to the nanoparticle. To ensure that the antigen binding site is exposed, the C-terminus of the antibody or antibody fragment is attached to the nanoparticle. Monoclonal antibodies can be used for this method. A feature of this method is the need for a mixture of at least two types of nanoparticles, each with a specific binding moiety, e.g., monoclonal antibody attached. The antibodies are directed...

...T2.

In another aspect of the invention, a polyclonal antibody can be attached to the nanoparticle. Since by definition these antibodies are multivalent, only a ...g., an antibody, in solution. In this assay, the antigen will be bound to the nanoparticle and placed into a sample. If an antibody directed to the antigen is present, binding... In another embodiment, the binding moiety can be a receptor-binding protein bound to the nanoparticle. When applied to a solution of cells, clustering of a cell surface receptor will result... A peptide sequence with a serine or tyrosine kinase recognition site is attached to a nanoparticle at one terminal end.

Addition of a solution containing a kinase will result in the... target molecules in a sample solution. The assay is based on the attachment to the nanoparticle of a natural or synthetic peptide that has an internal enzymatic site. Biotin is attached... internal hydrolytic sequence can have biotin attached to both termini. Avidin is attached to the nanoparticles and mixed with the biotinylated peptide in a sample. Since one avidin molecule binds four... decreased T2.

In another aspect of the invention, immediate aggregation is induced by attaching a nanoparticle to both termini of the peptide. The conjugate is placed in the sample and the... can form a dam methylation site (GATC).

The hybridization results in aggregation of the attached nanoparticle and a measurable decrease in T2. Upon contact with a methylase, the adenine and cytosine... restriction site (e.g., EcoRI, BamHI, PvuII) [1]. Hybridization of the oligonucleotides also aggregates the nanoparticles attached to the oligonucleotides resulting in a decreased T2. In this case, the - 41 presence described in the claims.

Example 1: Synthesis of SLipparamagnetic Iron Oxide Nanoparticles
Biocompatible, fluid phase magnetic nanoparticles (NH₂-CLIO) were synthesized as described and reacted with N-succinimidyl 3-(2-pyridyldithio)propionate... were synthesized using standard phosphoramidite chemistry (underlined bases will hybridize).

Example 3: Conjugation of Nanoparticles to Alkanethiol ... of conjugates was determined by light scattering (Coulter N4, Hialeah, FL).

Example 5: Use of Nanoparticle Conjugates in Turbid Media
Equimolar amounts in iron of oligonucleotide- nanoparticle conjugates denoted P1 and P2 were diluted in a 10% Fat Emulsion (Intralipid IO... turbid media.

Example 6: Based Assay
Example 6: A

Equimolar amounts in iron of oligonucleotide- **nanoparticles** denoted P1 and P2 were, diluted with 1 M NaCl in 0.1 M sodium...drops because T2 drops. This is due to a hybridization-induced formation of aggregates between oligonucleotide- **nanoparticle**. No binding occurs with non-complementary targets, and thus, there is no change in T2...and the mixture was incubated for 3.5 hours at room temperature. The avidin- CLIO **nanoparticle** was separated from unreacted avidin using a magnetic separation column (Miltényi Biotec, Auburn, CA). Iron...

...determined spectrophotometrically, and protein by the BCA method (Pierce). The number of avidins attached per **nanoparticle** was calculated using a molecular weight of 67 kDa for avidin and 2064 Fe atoms...46 Example 9: Assay for Protein (GFP) Using a Biotinylated Polyclonal Anti-GFP Avidin-CLIO **nanoparticles** made as described above were reacted with biotinylated polyclonal anti-GFP (Research Diagnostics Inc.) and...CTC-CTA-GGATC-CGC-ATT-(CH₂)₃-SH (SEQ ID NO: 17) were conjugated to **nanoparticles** as described in Example 3. The resulting - 47 conjugates (Magnetic Relaxation Switches, MRS), denoted P1...After a one-hour incubation with BaniHI, the aggregates were no longer present and monodisperse **nanoparticle** conjugates (50-60 run) were observed instead (FIG. 12b).

Example 12: Protein Assay Using Monoclonal Antibody-Nanoparticle Conjugates Monoclonal antibodies can be coupled to polymer coated magnetic **nanoparticles** using a variety of chemistries (see, e.g., Weissleder et al., U.S. Patent No...treatments with periodate. 48 In this assay format a P1 (first monoclonal attached to a **nanoparticle**) and P2 (second monoclonal attached to a **nanoparticle**) are synthesized in separate reactions. The target protein must contain epitopes for both monoclonals, so...

...in solution, the monoclonal antibodies will bind both epitopes on the antigen, thereby aggregating the **nanoparticles**, resulting in a decrease of T2.

OTHER EMBODIMENTS

It is to be understood that while the...

Claim

1 - An aggregate comprising a plurality of conjugates, wherein each conjugate comprises a magnetic **nanoparticle** linked to a binding moiety that specifically binds to a target molecule, to another binding... specifically bind to a target molecule, wherein each conjugate in the first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of first binding moieties that bind...

...site on the target molecule, and wherein each conjugate in the second population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind ...The composition of claim 14, wherein the conjugates further comprise functional groups that link the **nanoparticles** to the binding moieties.

16 The composition of claim 15, wherein the functional groups are...

...The composition of claim 15, wherein the conjugates further comprise a polymer associated with the **nanoparticles**, and wherein the functional groups are bound to the polymer and to the binding moieties...are oligonucleotides.

25 The composition of claim 24, wherein the oligonucleotides are attached to the **nanoparticles** by a single covalent bond at the 3' or 5' end of

each oligonucleotide.

26...

...antibodies.

28 The composition of claim 14, wherein the plurality is three binding moieties per **nanoparticle** .

52

. The composition of claim 14, wherein the magnetic metal oxide is a superparamagnetic metal...between about 15 and 100 nm-, sec

35 The composition of claim 14, wherein the **nanoparticle** is an amino-derivatized cross-linked iron oxide **nanoparticle** .

36 A conjugate comprising a magnetic **nanoparticle** linked to a first binding moiety, wherein the first binding moiety comprises a cleavage site...target molecule to form an aggregate, wherein each conjugate in the first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of first binding moieties that bind...

...site on the target molecule, and wherein each conjugate in the second population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind...are capable of forming an aggregate, wherein each conjugate in a first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a first binding moiety, wherein the first binding...target molecule in a sample, the method comprising
obtaining first and second populations of oligonucleotide- **nanoparticle** conjugates, wherein each conjugate in the first population comprises a **nanoparticle** having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the **nanoparticle** ; and wherein each conjugate in the second population comprises a **nanoparticle** having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle** ; wherein the first and second oligonucleotides are each complementary to first and second portions of...in the other populations; preparing a mixture of the first and second populations of oligonucleotide **nanoparticle** conjugates;
obtaining a fluid sample;
contacting the mixture with the sample under conditions that enable...
purifying a target molecule from a sample, the method comprising
obtaining a conjugate comprising a **nanoparticle** comprising a magnetic metal oxide linked by a cleavable bond to a binding moiety that...in a plurality of samples, the method comprising
obtaining first and second populations of oligonucleotide- **nanoparticle** conjugates, wherein each conjugate in the first population comprises a **nanoparticle** having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the **nanoparticle** , and wherein each conjugate in the second population comprises a **nanoparticle** having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle** ; wherein the first and second oligonucleotides are each complementary to first and second portions of...in the other populations; preparing a mixture of the first and second populations of

oligonucleotide
nanoparticle conjugates;
obtaining a plurality of fluid samples;
contacting a portion of the inixture with each...
...the samples to hybridize to the first and second oligonucleotides of
both populations of oligonucleotide- nanoparticle conjugates; and
simultaneously obtaining the relaxation properties of the fluid in each
of the plurality...administering to the subject at least one population
of conjugates, wherein each conjugate comprises a nanoparticle having a
magnetic metal oxide linked to a binding moiety
that specifically binds to the...

4/3,KWIC/32 (Item 15 from file: 349)
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00812595 **Image available**

PLASMA-DEPOSITED COATINGS, DEVICES AND METHODS
REVETEMENTS APPLIQUES PAR EXPOSITION A UN PLASMA, DISPOSITIFS ET PROCEDES
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Detailed Description

Detailed Description

... devices, a variety of other implantable structures, such as wires,
coils, sheets, pellets, particles, and nanoparticles, and the like, may
be treated with the gas plasma containing molecular species composed of

...9 4.21 2.8 4.6 2.5 2.2

7- n.d. = not detected

Stainless steel surfaces treated in a glow discharge of ammonia alone, that is without oxygen, did not have any detectable N₂, although a pronounced N₁ peak was found.

Collectively, the data from the ESCA analysis of the surfaces exposed to ammonia/oxygen demonstrate that two types of chemical state of nitrogen are being deposited.

EXAMPLE13

Stainless...

4/3,KWIC/33 (Item 16 from file: 349)

DIALOG(R) File 349:PCT FULLTEXT

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00557479

CONDUCTIVE ORGANIC SENSORS, ARRAYS AND METHODS OF USE

CAPTEURS ORGANIQUES CONDUCTEURS, MOSAÏQUE DE CAPTEURS ET PROCÉDES D'EMPLOI

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Detailed Description

Detailed Description

... In certain other embodiments, the conductive material is a conductive particle, such as a colloidal nanoparticle. As used herein the term "nanoparticle" refers to a conductive cluster, such as a metal cluster, having a diameter on the nanometer scale. Such nanoparticles are optionally stabilized with organic ligands.

Examples of colloidal nanoparticles for use in accordance with the present invention are described in the literature.

In this...

...can optionally be a ligand that is attached to a central core making up the nanoparticle. These ligands i.e., caps, can be polyhomo- or polyhetero-functionalized, thereby being suitable for detecting a variety of chemical analytes. The nanoparticles, i.e., clusters, are stabilized by the attached

ligands. in certain embodiments, the conducting component of the resistors are **nanoparticles** comprising a central core conducting element and an attached ligand optionally in a polymer matrix...

...2, various conducting materials are suitable for the central core. In certain preferred embodiments, the **nanoparticles** have a metal core.

Preferred metal cores include, but are not limited to, Au, Ag, Pt, Pd, Cu, Ni, AuCu and regions thereof. Gold (Au) is especially preferred. These metallic **nanoparticles** can be synthesized using a variety of methods. In a preferred method of synthesis, a...of combinations of 10-20 polymers can be readily fabricated.

51

The resistors can include **nanoparticles** comprising a

4

central core conducting element and an attached ligand, with these **nanoparticles** dispersed in a semiconducting or conducting organic matrix. With reference to Table 2, various conducting materials are suitable for the central core. In certain embodiments, the **nanoparticles** have a metal core.

Examples of metal cores include, but are not limited to, Au, Ag, Pt, Pd, Cu, Ni, AuCu and regions thereof. These metallic **nanoparticles** can be synthesized using a variety of methods.

In one method of synthesis, a modification...

...gold clusters having a core dimension of about 1 nm to about 100 nm. The **nanoparticles** range in size from about 1 nm to about 50 nm, but may also range...

...ratio

of H₂AuCl₄ to alkanethiol, it is possible to generate various sizes and dimensions of **nanoparticles** suitable for a variety of analytes. Although not intending to be bound by any particular...

...ligand

monolayer in a controlled fashion. Using this reaction, it is then possible to generate **nanoparticles** of exacting sizes and dimensions.

In certain other embodiments, sensors are prepared as composites of "naked" **nanoparticles** and a semiconducting or conducting organic material is added. As used herein, the term "naked **nanoparticles** " means that the core has no covalently attached ligands or caps. A wide variety of...1 and 1 ppm and pristine emeraldine salt chemiresistive detectors have been reported to have **detection** thresholds of 1 ppm to ammonia . Furthermore, the ES-DBSA(1:0.5)/CB responses were pseudo-reversible (see Figure 2...in a conductive poly(3-hexylthiophene) containing gold salts as the counterion and Au (0) **nanoparticles** as the conductive filler.

Poly (3 -hexyl thi ophene) /Pt

Detector 5 - Similar to the...

...in a
conductive poly(3-hexylthiophene) containing platinum salts as
the counterion and Pt (0) nanoparticles as the conductive
filler.

Charge transfer saltsICarbon black

Detector 6 - (a) A total weight of...

4/3,KWIC/34 (Item 17 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00461348

POLYHYDROXYALKANOATES FOR i(IN VIVO) APPLICATIONS

POLYHYDROXYALCANOATES DESTINES A DES APPLICATIONS i(IN VIVO)

Patent Applicant/Assignee:

METABOLIX INC,

Inventor(s):

WILLIAMS Simon F,

MARTIN David P,

GERNGROSS Tillman,

HOROWITZ Daniel M,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9851812 A2 19981119

Application: WO 98US9834 19980512 (PCT/WO US9809834)

Priority Application: US 9746211 19970512; US 9754289 19970731; US
9763501 19971024; US 9765921 19971117

Designated States:

(Protection type is "patent" unless otherwise stated - for applications
prior to 2004)

AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 14204

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... hydrogen peroxide.

The latex may contain particles of any size, although the particles are
preferably nanoparticles and/or microparticles. The latex particles may
be crystalline or amorphous, but are more preferably...film surface was
washed with water, quenched with glycine and blocked
with 0.1 % gelatin. Detection with a strepavidin horseradish
peroxidase
conjugate and a chemiluminescent HRP detection solution demonstrated
biotin modification of the surface. A PHO film without ammonia gas
plasma treatment was used as a control and demonstrated no biotin
modification under identical...

Claim

... The method of claim 17 wherein the device is in the form
of microparticles or nanoparticles .

SUBSTITUTE SHEET (RULE 26)

. The method of claim 17 wherein the device comprises a
material...The device of claim 41 wherein the device is in the form of
microparticles or nanoparticles .

47 The device of claim 41 wherein the device comprises a material selected from the...

4/3,KWIC/35 (Item 18 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00314583

IMMOBILIZATION OF BIOLOGICALLY ACTIVE MATERIALS AND DIAGNOSTIC AGENTS IN
CROSS-LINKED POLY(ORGANOPHOSPHAZENES)
IMMOBILISATION DE SUBSTANCES ET D'AGENTS DE DIAGNOSTICS BIOLOGIQUEMENT
ACTIFS AU SEIN DE POLY(ORGANOPHOSPHAZENE) RETICULES

Patent Applicant/Assignee:

THE PENN STATE RESEARCH FOUNDATION,

Inventor(s):

ALLCOCK Harry R,
PUCHER Shawn R,
VISSCHER Karyn B,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9532736 A1 19951207

Application: WO 95US6854 19950531 (PCT/WO US9506854)

Priority Application: US 94251510 19940531

Designated States:

(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AU CA JP KR NO AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 12609

Fulltext Availability:

Detailed Description

Detailed Description

... 8 having a temperature
of between about 250C and 370C.

As used herein, the term **nanoparticle** or nanosphere typically refers to a particle, usually a solid particle (as opposed to a capsule), of size ranging from 10 to 1000 nm. In a preferred embodiment, the **nanoparticle** is biodegradable, biocompatible, has a size of less than 200 nm and has a rigid...and those applications that do not require high enzyme activity (for example, an assay to **detect** urea as opposed to a method to convert all urea to **ammonia**). For those applications, the meaning of a "significant amount of enzyme activity" must be considered...tract) or by inhalation.

The polymers disclosed herein can be fabricated into loaded microparticles or **nanoparticles** using any appropriate method known to those skilled in the art.

In one embodiment, the...

4/3,KWIC/36 (Item 1 from file: 654)

DIALOG(R) File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6465225

UTILITY

Nanosensors based on functionalized nanoparticles and Surface Enhanced Raman Scattering

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Laurence, Ted A., Livermore, CA, US

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94551, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060050268	A1	20060309	US 2004935783	20040907

Fulltext Word Count: 6327

Nanosensors based on functionalized nanoparticles and Surface Enhanced Raman Scattering

Abstract:

...signals of several orders of magnitude. When molecules of interest are attached to designed metal **nanoparticles**, a SERS signal is attainable with single molecule detection limits. This provides an ultrasensitive means of detecting the presence of molecules. By using selective chemistries, metal **nanoparticles** can be functionalized to provide a unique signal upon analyte binding. Moreover, by using measurement techniques, such as, ratiometric received SERS spectra, such metal **nanoparticles** can be used to monitor dynamic processes in addition to static binding events. Accordingly, such **nanoparticles** can be used as nanosensors for a wide range of chemicals in fluid, gaseous and...

Summary of the Invention:

...groups (e.g., thiol-groups). Additional improvement in signal-to-noise occurs because the conducting **nanoparticles** tend to quench any natural fluorescence produced by the molecules. These increases in Raman signal...

...9): p. 1667-1670; Nie, S. and S. R. Emory, Probing Single Molecules and Single **Nanoparticles** by Surface-Enhanced Raman Scattering. Science, 1997. 275: p. 1102-1106]. This extraordinary increase in...SERS-based detection method that includes providing one or more nanosensors, each having a metal **nanoparticle** covalently bonded to one or more Raman-active molecules. By measuring ratiometric signals of a...

Description of the Invention:

...0019] FIG. 2 shows SERS spectra of functionalized 4-MBA **nanoparticles** indicating pH sensitivity...atomic force microscope image of Chinese Hamster Ovary Cells (CHO) after passive uptake of

functionalized nanoparticles .

[...atomic mass units that are operatively coupled (e.g., by covalence bonding) to a metal nanoparticle 's surface. Such changes can be reversible (e.g., changes in the local environment, such...

- ...0030] By utilizing such designed nanosensors (i.e., herein meaning Raman active molecules coupled to nanoparticles) with detection means as disclosed herein, the ...0033] Nanosensors 12 having individual nanoparticles and/or small clusters of nanoparticles as the sensor element are designed to scatter radiation facilitated by the excitation of plasmon modes produced on the surface of the nanoparticles . Element 8 can additionally operate as a means to collect scattered surface enhanced plasmon radiation...about 1000 atomic mass units. Such nanosensors are often coupled by covalence bonding to metal nanoparticles such as gold, silver, copper and platinum, often having a size range from about 5...
- ...functionality (i.e., for targeting specific chemicals, biological substances, etc.) are often attached to the nanoparticles using thiol chemistry to provide independent marker and reference modes and the specific functional modes...
- ...0035] Nanoparticles as disclosed herein, which are coupled to the molecules, can be spherical, rodlike, cubic, triangular...
- ...plasmon resonance at an excitation wavelength between about 400 nm and about 1000 nm. Such nanoparticles can be attached to substrate surfaces as sensors or assays and they can be attached to such surfaces in random or regular arrays as single particles or nanoparticle clusters of functionalized nanoparticles . Each such cluster can be coated with a highly specific functional group for a different etc. Such an array can be produced, for example, by inkjet-printing functionalized nanoparticles onto an inert surface or alternately by incorporating such nanoparticles into a supporting medium, such as an aerogel or polymer matrix...
- ...detector for color analysis of the colorimetric shift of the surface plasmon resonance of the nanoparticles while an atomic force microscope capable of being adapted with the invention, as shown in FIG. 1, can be utilized to image configured nanoparticles so as to aid in the analysis of resultant SERS spectra and/or response. In addition, functionalized nanoparticle clusters having functionality for a wider range of chemicals can be configured as nanosensors to...as being disposed in solution as shown in FIG. 1. By such an arrangement, functionalized nanoparticles of the present invention can be used to detect specific molecular species or can be...
- ...or class of molecules. Moreover, such nanosensors as disclosed herein can be configured having "unfunctionalized" nanoparticles , i.e., they can be configured to detect molecules that attach to a nanoparticle 's surface through a non-specific interaction, often by electrical charge interaction so as to...
- ...magnetic core and utilized as an active collector. By incorporating a magnetic core into the nanoparticles that make up the nanosensors as disclosed herein, they can be added to a solution...Methyl Mercaptan, Nitrogen Dioxide, Parathion, Phosgene, Phosphine; Sulfur Dioxide, Toluene diisocyanate, Allyl Alcohol, Acrolein, Acrylonitrile, Ammonia , Arsine, Chlorine, Diborane, Ethylene Oxide, Formaldehyde, Hydrogen Bromide, Hydrogen Cyanide, Hydrogen Selenide, and Hydrogen sulfide. Sensor molecules for the detection of such substances can include, but are not

limited to, lanthanides, multi-dentate chelates (e...beneficial example application of the present invention, a SERS spectrum produced by nanosensors of individual nanoparticle clusters, such as, but not limited to silver nanoclusters, which are functionalized by adding, for ...

...of a 30 mM methanol solution of 4-mercaptobenzoic (hereafter 4-MBA) to an aqueous nanoparticle solution, can be utilized to respond to the pH changes of a surrounding medium in...

...as measured by the example embodiment, as shown in FIG. 1, using 4-MBA functionalized nanoparticles as the nanosensors. The most prominent features in such spectra are ring breathing modes 1077...0048] Moreover, by utilizing individual nanoparticles and/or small nanoclusters (e.g., nanoparticles and/or clusters having dimensions between about 5 nm and 1 [small mu, Greek]m more often between about 50 nm and 100 nm), such nanoparticles and/or nanoclusters can also be arranged as sensors inside single living cells. Such sizes of the nanoparticles and/or clusters combined with the highly localized probe volume inherent to SERS make such resultant nanosensors particularly beneficial for monitoring biological processes in vivo. Functionalized nanoparticles to be used as a probe can be micro-injected into cells or the cells can be forced to take nanoparticles up passively (e.g., phagocytosis) or by ultra-sonification and/or electroporation of the cells0049] FIG. 6a and FIG. 6b illustrate passive uptake of nanosensors having functionalized nanoparticles by Chinese Hamster Ovary cells (CHO). FIG. 6a shows a confocal microscope image produced by...

...areas within encircled regions 630) after incubation for 24 hours with 4-MBA coated silver nanoparticles . FIG. 6b shows a SERS spectra 634 representative of 4-MBA obtained from a nanosensor...

Exemplary or Independent Claim(s):

...each said nanosensor further comprising: at least one Raman-active molecule coupled to a metal nanoparticle and configured to produce a SERS spectra; and means for monitoring ratiometric signals of said...

...each said nanosensor further comprising: at least one Raman-active molecule coupled to a metal nanoparticle ; an electromagnetic radiation source; means configured to direct said electromagnetic radiation source onto disposed said...

...based detection method, comprising: providing one or more nanosensors, each said nanosensor comprising: a metal nanoparticle covalently bonded to one or more Raman-active molecules; measuring ratiometric signals

Non-exemplary or Dependent Claim(s):

...8. The apparatus of claim 1, wherein said metal nanoparticle has a size range between about 5 nm and about 1 [small mu, Greek]m apparatus of claim 1, wherein said metal nanoparticle further comprises a magnetic core...24. The system of claim 17, wherein said metal nanoparticle has a size range between about 5 nm and about 1 [small mu, Greek]m...

...25. The system of claim 17, wherein said metal nanoparticle further comprises a magnetic core...40. The method of claim 33, wherein said

metal nanoparticle has a size range between about 5 nm and about 1
[small mu, Greek]m...

...41. The method of claim 33, wherein said metal nanoparticle further
comprises a magnetic core...

4/3,KWIC/37 (Item 2 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6431626

Derwent Accession: 2005-615498

UTILITY

Carbon nanotube based resonant-circuit sensor

Inventor: Rao, Apparao M., Anderson, SC, US

Chopra, Saurabh, Raleigh, NC, US

Assignee: Clemson University, (02), Clemson, SC, US

Examiner: Williams, Hezron

Assistant Examiner: Bellamy, Tamiko

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6997039	B2	20060214	US 2004785421	20040224
Related Publ	US 20050183492	A1	20050825		

Fulltext Word Count: 8508

Summary of the Invention:

...0007] Chopra, et al. ("Carbon-nanotube-based Resonant-circuit
Sensor for Ammonia," Applied Physics Letters, Volume 8, Number 24,
2002, which is incorporated herein in its entirety by reference thereto)
have described an ammonia sensor formed of a simple micro-strip
circular disk resonator coated with carbon nanotubes (either
single-walled or multi-walled nanotubes) on the surface. The sensors
show a shift in resonant frequency upon adsorption of ammonia of about
4.375 MHz for a single-walled nanotube (SWNT) sensor and a shift of
about 3.25 MHz for a multi-walled nanotube (MWNT) sensor, and can
detect the presence of ammonia down to a concentration of about 100
ppm...ferrocene mixture. The xylene serves as the hydrocarbon source and
ferrocene provides the iron catalyst nanoparticles that can seed the
nanotubes that are grown. According to one process, ferrocene
(approximately 6...including non-polar and inert gases, for example, but
in addition, the sensitivity of the sensors can be greatly increased.
For example, when considering the detection of the polar gas ammonia,
when utilizing a resonant sensor of the disclosed invention including a
layer of SWNT as-prepared (that is, formed in air and not degassed
following formation) the sensor can detect the presence of ammonia
down to a concentration of about 100 ppm. In contrast, following a
degassing procedure such as that outlined above, the disclosed sensors
can detect the presence of ammonia down to a concentration of about
100 ppb...those embodiments wherein as-prepared nanotubes are applied to
the resonator and utilized for the detection of materials, such as
polar gases like ammonia or organic vapors, the initial resonant
frequency of the resonator can often be recovered within...to the
presence of polar gases. FIG. 8 shows the response of a SWNT-containing
sensor to ammonia and carbon monoxide. The first curve (solid line) is

the response of the sensor in air with a resonant frequency of 3.887 GHz. The second curve (squares) is 0065] The fourth curve (crosses) shows the response of the SWNT sensor to ammonia. The resonant frequency shift in the case of ammonia exposure is slightly greater than that for carbon monoxide, which can be explained due to...

...to different environmental conditions. As the as-prepared sample is degassed, the conductivity of the sensor increases, which is evident from the increase in the Q-factor of the sensor. Upon exposure of the sample to ammonia and carbon monoxide, the conductivity of the sensor decreases to a greater extent than when it was exposed to oxygen...

4/3,KWIC/38 (Item 3 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6369151 **IMAGE Available
Derwent Accession: 2004-460456

UTILITY

Nanostructure sensor device with polymer recognition layer

Inventor: Star, Alexander, Albany, CA, US
Gabriel, Jean-Christophe P., Pinole, CA, US
Gruner, George, Los Angeles, CA, US

Assignee: Unassigned

Correspondence Address: BRIAN M. BERLINER; O'MELVENY & MYERS LLP, 400 SOUTH HOPE STREET, LOS ANGELES, CA, 90071-2899, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050279987	A1	20051222	US 2003656898	20030905
Provisional				US 60-408547	20020905

Fulltext Word Count: 3105

Summary of the Invention:

...nanotubes grown on silicon or other substrates by chemical vapor deposition from iron-containing catalyst nanoparticles with methane/hydrogen gas mixture at 900 degree C. Other catalyst materials and gas mixtures...

Description of the Invention:

...shown in FIGS. 5A and 5B, respectively. The response and recovery of the PEI-functionalized ammonia sensor (FIG. 5B) are remarkably fast. The response to ammonia is also dependent on a gate voltage. At positive gate, measured current through the PEI...

Non-exemplary or Dependent Claim(s):

...9. The nanostructure sensor of claim 1, wherein the target species comprises ammonia and the polymer layer is PEI...

4/3,KWIC/39 (Item 4 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

6320940 **IMAGE Available

Derwent Accession: 2005-784098

UTILITY

Chemical sensor using semiconducting metal oxide nanowires

Inventor: Zhou, Chongwu, Rowland Heights, CA, US

Assignee: Unassigned

Correspondence Address: FISH & RICHARDSON, PC, 12390 EL CAMINO REAL, SAN
DIEGO, CA, 92130-2081, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050247961	A1	20051110	US 200577164	20050309
Provisional				US 60-551840	20040309

Fulltext Word Count: 4287

Description of the Invention:

...solid growth technique may be used in which the nanowire diameters are controlled by catalyst nanoparticle size. Another technique may use a template assisted approach with porous silica...upon NH₃ exposure. In summary, the performance of the Indium oxide nanowire as ammonia sensors is affected by both the doping concentration and surface preparation. For example, the surfaces may...

4/3,KWIC/40 (Item 5 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6227301

Derwent Accession: 2005-417822

UTILITY

Polymer compositions and methods for their use

Inventor: Hunter, William L., Vancouver, CA
Toleikis, Philip M., Vancouver, CA
Gravett, David M., Vancouver, CA
Maiti, Arpita, Vancouver, CA
Liggins, Richard T., Coquitlam, CA
Takacs-Cox, Aniko, North Vancouver, CA
Avelar, Rui, Vancouver, CA
Loss, Troy A. E., North Vancouver, CA

Assignee: Angiotech International AG, (03), Zug, CH

Correspondence Address: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050186244	A1	20050825	US 20041790	20041202
Continuation	PENDING			US 2004996354	20041122
CIP	PENDING			US 2004986231	20041110
Provisional				US 60-611077	20040917
Provisional				US 60-586861	20040709
Provisional				US 60-566569	20040428
Provisional				US 60-526541	20031203
Provisional				US 60-525226	20031124
Provisional				US 60-523908	20031120

Fulltext Word Count: 335461

Description of the Invention:

...salts, and also salts with physiologically tolerable quaternary ammonium ions and acid addition salts with ammonia and physiologically tolerable organic amines such as, for example, triethylamine, ethanolamine or tris-(2-hydroxyethyl...

4/3,KWIC/41 (Item 6 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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6224549 **IMAGE Available

Derwent Accession: 2005-615498

UTILITY

Carbon nanotube based resonant-circuit sensor

Inventor: Rao, Apparao M., Anderson, SC, US

Chopra, Saurabh, Raleigh, NC, US

Assignee: Clemson University, (02)

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GREENVILLE, SC, 29602-1449, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050183492	A1	20050825	US 2004785421	20040224

Fulltext Word Count: 8168

Summary of the Invention:

...0007] Chopra, et al. ("Carbon-nanotube-based Resonant-circuit Sensor for Ammonia," Applied Physics Letters, Volume 8, Number 24, 2002, which is incorporated herein in its entirety by reference thereto) have described an ammonia sensor formed of a simple micro-strip circular disk resonator coated with carbon nanotubes (either single-walled or multi-walled nanotubes) on the surface. The sensors show a shift in resonant frequency upon adsorption of ammonia of about 4.375 MHz for a single-walled nanotube (SWNT) sensor and a shift of about 3.25 MHz for a multi-walled nanotube (MWNT) sensor, and can detect the presence of ammonia down to a concentration of about 100 ppm...

Description of the Invention:

...ferrocene mixture. The xylene serves as the hydrocarbon source and ferrocene provides the iron catalyst nanoparticles that can seed the nanotubes that are grown. According to one process, ferrocene (approximately 6...including non-polar and inert gases, for example, but in addition, the sensitivity of the sensors can be greatly increased. For example, when considering the detection of the polar gas ammonia, when utilizing a resonant sensor of the disclosed invention including a layer of SWNT as-prepared (that is, formed in air and not degassed following formation) the sensor can detect the presence of ammonia down to a concentration of about 100 ppm. In contrast, following a degassing procedure such as that outlined above, the disclosed sensors can detect the presence of ammonia down to a concentration of about 100 ppb...those embodiments wherein as-prepared nanotubes are applied to the resonator and utilized for the detection of materials, such as polar gases like ammonia or organic vapors, the initial resonant frequency of the resonator can often be recovered within...to the

presence of polar gases. FIG. 8 shows the response of a SWNT-containing sensor to ammonia and carbon monoxide. The first curve (solid line) is the response of the sensor in air with a resonant frequency of 3.887 GHz. The second curve (squares) is...0065] The fourth curve (crosses) shows the response of the SWNT sensor to ammonia. The resonant frequency shift in the case of ammonia exposure is slightly greater than that for carbon monoxide, which can be explained due to is degassed, the conductivity of the sensor increases, which is evident from the increase in the Q-factor of the sensor. Upon exposure of the sample to ammonia and carbon monoxide, the conductivity of the sensor decreases to a greater extent than when it was exposed to oxygen...

4/3,KWIC/42 (Item 7 from file: 654)
 DIALOG(R)File 654:US Pat.Full.
 (c) Format only 2006 Dialog. All rts. reserv.

6220053

Derwent Accession: 2005-396175

UTILITY

Polymer compositions and methods for their use

Inventor: Hunter, William L., Vancouver, CA
 Toleikis, Philip M., Vancouver, CA
 Gravett, David M., Vancouver, CA
 Maiti, Arpita, Vancouver, CA
 Liggins, Richard T., Coquitlam, CA
 Takacs-Cox, Aniko, North Vancouver, CA
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 Loss, Troy A. E., North Vancouver, CA

Assignee: Angiotech International AG, (03), Zug, 6304, CH

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	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	----	-----	-----
Main Patent	US 20050182463	A1	20050818	US 20041788	20041202
Continuation	PENDING			US 2004996354	20041122
CIP	PENDING			US 2004986231	20041110
Provisional				US 60-611077	20040917
Provisional				US 60-586861	20040709
Provisional				US 60-566569	20040428
Provisional				US 60-526541	20031203
Provisional				US 60-525226	20031124
Provisional				US 60-523908	20031120

Fulltext Word Count: 335495

Description of the Invention:

...salts, and also salts with physiologically tolerable quaternary ammonium ions and acid addition salts with ammonia and physiologically tolerable organic amines such as, for example, triethylamine, ethanolamine or tris-(2-hydroxyethyl)...

4/3,KWIC/43 (Item 8 from file: 654)
 DIALOG(R)File 654:US Pat.Full.
 (c) Format only 2006 Dialog. All rts. reserv.

6209949

Derwent Accession: 2005-396175

UTILITY

Polymer compositions and methods for their use

Inventor: Hunter, William L., Vancouver, CA
Toleikis, Philip M., Vancouver, CA
Gravett, David M., Vancouver, CA
Maiti, Arpita, Vancouver, CA
Liggins, Richard T., Coquitlam, CA
Takacs-Cox, Aniko, North Vancouver, CA
Avelar, Rui, Vancouver, CA
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050175665	A1	20050811	US 20046896	20041207
Continuation	PENDING			US 2004996354	20041122
CIP	PENDING			US 2004986231	20041110
Provisional				US 60-611077	20040917
Provisional				US 60-586861	20040709
Provisional				US 60-566569	20040428
Provisional				US 60-526541	20031203
Provisional				US 60-525226	20031124
Provisional				US 60-523908	20031120

Fulltext Word Count: 334757

Description of the Invention:

...salts, and also salts with physiologically tolerable quaternary ammonium ions and acid addition salts with ammonia and physiologically tolerable organic amines such as, for example, triethylamine, ethanolamine or tris-(2-hydroxyethyl...

4/3,KWIC/44 (Item 9 from file: 654)

DIALOG(R) File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6113955 **IMAGE Available

Derwent Accession: 2005-455412

UTILITY

Methods for deposition of sensor regions onto optical storage media substrates and resulting devices

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Boyette, Scott Martell, New Hope, PA, US
Leach, Andrew Michael, Clifton Park, NY, US
Krishnan, Kasiraman, Clifton Park, NY, US

Assignee: Unassigned

Correspondence Address: GE Global Research;Docket Room K-1/4A59, One
Research Circle, Niskayuna, NY, 12309, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20050112358	A1	20050526	US 2003723536	20031124

Fulltext Word Count: 15330

Description of the Invention:

...0018] FIG. 9 is a graph depicting the response of three **sensor** regions as recorded using an optical drive. Different **sensor** regions were exposed to saturated **ammonia** vapor for different amounts of time ($t_1 < t_2 < t_3$...chemical and biological species. Analyte-specific reagents include organic and inorganic dyes and pigments, nanocrystals, **nanoparticles**, quantum dots, organic fluorophores, inorganic fluorophores and similar materials...0067] As noted above, the analyte-specific reagents also include nanocrystals, **nanoparticles** and quantum dots and are known to those skilled in the art. Suitable nanocrystals include...

...not limited to, those made of MoS_2 , ZnO, Si, CdTe, and Ge. Suitable **nanoparticles** include, but are not limited to, those made of Cu, SiO_2 , and LaB...

...where a pH sensitive reagent such as bromothymol blue or bromocresol green is used, the **sensor** spot can be exposed to vapor or liquids which may include **ammonia** and the **sensor** read to confirm the presence of and the amounts of such an alkaline vapor. Such...exposure times from 0 to about 20 seconds. FIG. 9 shows the response of three **sensor** regions as recorded using an optical drive (LG Electronics, Inc., Model GCC4480B) where different **sensor** regions were exposed to saturated **ammonia** vapor for different amounts of time ($t_1 < t_2 < t_3$...

Non-exemplary or Dependent Claim(s):

...analyte-specific reagent is selected from the group consisting of organic dyes, inorganic dyes, nanocrystals, **nanoparticles**, quantum dots, organic fluorophores, inorganic fluorophores, IR absorbing dyes, near infrared absorbing materials, UV absorbing...

...an analyte-specific reagent selected from the group consisting of organic dyes, inorganic dyes, nanocrystals, **nanoparticles**, quantum dots, organic fluorophores, inorganic fluorophores, IR absorbing dyes, UV absorbing dyes, photochromic dyes, and...

...an analyte-specific reagent selected from the group consisting of organic dyes, inorganic dyes, nanocrystals, **nanoparticles**, quantum dots, organic fluorophores, inorganic fluorophores, IR absorbing dyes, UV absorbing dyes, photochromic dyes, and...

4/3,KWIC/45 (Item 10 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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6113682 **IMAGE Available

Derwent Accession: 2005-372031

UTILITY

Odor controlling article including a visual indicating device for monitoring odor absorption

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	Publication Number	Kind	Date	Application Number	Filing Date
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Main Patent	US 20050112085	A1	20050526	US 2003687269	20031016

Fulltext Word Count: 7232

Summary of the Invention:

...substance, compound, chemical, mixture or absorbent (such as activated carbon, clay, zeolites, coated or modified nanoparticle silica or alumina and molecular sieves) useful in controlling odors...

...silicates, starches, ion exchange resins, cyclodextrins, molecular sieves or high surface area materials such as nanoparticles (see, for example, EP-A-348 978, EP-A-510619, WO 91/12029, WO 91...

Description of the Invention:

...0025] FIG. 2 shows a standard curve for the detection of ammonia by BDMB...

...per billion (ppb), more preferably from >10 ppb, and most preferably >100 ppb) of amines, ammonia, sulfur compounds, carboxylic acids and aldehydes were identified (Table 3). While the indicating agent may not detect the lower levels of odorous compounds immediately, it may change color in response to these...

...0036] Although the odor absorbing agents which are specifically mentioned in the examples below are nanoparticles from Nissan Chemical America Corporation of Houston, Tex. and Michler's Hydrol from Aldrich Chemical...

...molecular sieves, which are known in the art, and other high surface area materials or nanoparticles may also be used as the odor absorbing agent...

...0037] The nanoparticles used in the practice of this invention can act as carriers for at least one metal ion present on the surface of the nanoparticle, and the metal ion creates an active site that binds with at least one gaseous compound and/or odorous compound thereby removing the compound from the surrounding environment. Nanoparticles can also absorb certain gaseous compounds and/or odorous compounds from the surrounding environment by adsorption directly onto the surface of the nanoparticles.

[...]

...0038] The nanoparticles are modified with metal ions that ionically bond with compounds such as gases and odorous...

...on the periodic table. Other ions can be used in the invention as well. The nanoparticle may be made from any of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold...

...0039] Modified nanoparticles are made by mixing nanoparticles with solutions containing metal ions. Such solutions are generally made by dissolving metallic compounds into...

...metal ions in the solution. The metal ions are drawn to and adsorbed onto the nanoparticles due to the electric potential differences. Further discussion of the modification of nanoparticles may be found in U.S. patent application Ser. No. 10/137,052, filed on...

...0043] The use of pH control in the modification of silica nanoparticles was demonstrated using a 10 weight percent suspension of SNOWTEX-OXS(R) nanoparticles from Nissan Chemical, having an unmodified particle size of 4 to 6 nm. The pH...

...Zeta potential was obtained the addition of copper chloride was stopped. The resulting copper modified nanoparticle had a particle size of about 43 nm and a surface area of about 500...

...and air-dry method. The odor absorbing agents for this example were alumina-coated silica nanoparticles SNOWTEX-AK(R), available from Nissan Chemical...

...shown in FIG. 2, a standard curve was derived using ammonium hydroxide solution as an ammonia odor source detected by BDMB (MH-dye). In FIG. 2 the x-axis is the concentration of ammonia in ppb from 0 to 400 and the y-axis is the absorbance at 590...

...Technologies of Chantilly, Va. (Model # MRX). The absorbance readings were plotted against the concentrations of ammonia solutions, with the concentrations being represented as parts per billion (ppb). The sensitivity of ammonia detection was very high according to the MH-dye method, and it was shown that the...

...0082] SNOWTEX-C(R) silica nanoparticles from Nissan Chemical were modified by placing 20 mg copper chloride in 20 ml of a 20% wt/wt SNOWTEX-C(R) nanoparticle suspension. KIMWIPES(R) tissues from Kimberly-Clark Corporation were coated with the copper ion modified silica nanoparticle suspension and allowed to air dry. These light green colored KIMWIPES(R) tissues were placed

Exemplary or Independent Claim(s):

...15. An article for controlling odor comprising a nanoparticle selected from the group consisting of silica, alumina, magnesium oxide, titanium dioxide, iron oxide, gold...

4/3,KWIC/46 (Item 11 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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6070376 **IMAGE Available

Derwent Accession: 2005-331557

UTILITY

Visual indicating device for bad breath

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Publication

Application

Filing

	Number	Kind	Date	Number	Date
Main Patent	US 20050085739	A1	20050421	US 2003687270	20031016

Fulltext Word Count: 6930

Description of the Invention:

...0023] FIG. 2 shows a standard curve for the detection of ammonia by MH-dye...

...0031] The invention provides simple visual breath testing devices which are able to detect levels of sulfur and/or ammonia compounds in a user's breath which are indicative of bad breath. Thus, the breath...

...0037] The substrate, typically a cellulose tissue, may be coated with nanoparticles to provide a high surface area coating on the substrate, i.e., higher than the...

...cellulose tissue may be given a boost in surface area by coating it with the nanoparticles. The treated substrate may be then coated with the visual indicating dye. It's believed...

...0038] The average size of the nanoparticles is generally less than about 100 nanometers, in fact it may be from about 1...

...0039] The nanoparticles may have a surface area of from about 50 square meters per gram (m²sup...)

...0040] In addition, the nanoparticles may also be relatively nonporous or solid. That is, the nanoparticles may have a pore volume that is less than about 0.5 milliliters per gram...

...g. It is believed that the solid nature, i.e., low pore volume, of the nanoparticles may enhance the uniformity and stability of the nanoparticles.

[...]

...0041] Examples of commercially available alumina nanoparticles include, for instance, Aluminasol(R) 100, Aluminasol(R) 200 and Aluminasol(R) 520, which are available from Nissan Chemical America Corporation, Houston, Tex., USA. Alternatively, silica nanoparticles may be utilized, such as Snowtex-C(R), Snowtex-O(R), Snowtex-PS(R) and Snowtex-OXS(R) nanoparticles, which are also available from Nissan Chemical...

...0042] Snowtex-OXS(R) nanoparticles, for instance, have a particle size of from 4 to 6 nanometers, and may be...

...per gram. Also, alumina-coated silica particles may be used, such as Snowtex-AK(R) nanoparticles available from Nissan Chemical...

...tissues from Kimberly-Clark Corporation of Dallas, Tex., USA were coated with Snowtex-O(R) nanoparticles (pH 4.1), available from Nissan Chemical, and were used in the examples described herein...

...mg/ml stock solution of MH-dye 16 was applied on a Snowtex(TM)-O nanoparticle-coated Scott(R) paper towel and allowed to air dry. The dye-coated paper towel...

...0082] KIMWIPES(R) tissues were coated with a 5% Snowtex-O(R) nanoparticle solution from Nissan Chemical and then air-dried. 5.0 mg/ml stock solution of MH-dye in acetonitrile was applied to the Snowtex-O(R) nanoparticle-coated KIMWIPES(R) tissues and a blue color was observed to develop as the applied...

...Oakland, Calif., was placed on a cardboard strip 22, and a piece of the dye-nanoparticle coated tissue 24 was placed over a first end 25 of the straw 20. Thus...

...1 mg/ml stock solution of MH-dye was applied on a Snowtex(R)-O nanoparticle-coated Scott(R) paper towel and allowed to air dry, before being attached to the

Exemplary or Independent Claim(s):

...23. A breath testing device comprising nanoparticles and a visual indicating agent that is color sensitive to at least one odorous compound...

...portion defining a passage that is open at least one end, wherein the device contains nanoparticles and a visual indicating agent that is color sensitive to at least one odorous compound...

...or into a carrier portion of a breath testing device, the breath testing device containing nanoparticles and a visual indicating agent that is sensitive to at least one odorous compound; and...

Non-exemplary or Dependent Claim(s):

...29. The breath testing device of claim 23, wherein the nanoparticles have an average size of less than about 100 nanometers...

...30. The breath testing device of claim 23, wherein the nanoparticles have an average size of from about 1 to about 50 nanometers...

...31. The breath testing device of claim 23, wherein the nanoparticles have a surface area of from about 50 to about 1000 square meters per gram...

...32. The breath testing device of claim 23, wherein the nanoparticles have an average size of from about 100 to about 600 square meters per gram...

...33. The breath testing device of claim 23, wherein the nanoparticles include silica, alumina, or combinations thereof...

4/3,KWIC/47 (Item 12 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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6050494 **IMAGE Available

Derwent Accession: 2003-493444

UTILITY

Use of id semiconductor materials as chemical sensing materials, produced and operated close to room temperature

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Main Patent	US 20050072213	A1	20050407	US 2002496380	20021126
PCT	WO 2002EP13309		20021126		
Priority				EP 2001128064	20011126

Fulltext Word Count: 11271

Abstract:

...1), a sensor medium (3) formed on the substrate, the sensor medium comprising one-dimensional **nanoparticles**, wherein the one-dimensional **nanoparticles** essentially consist of a semiconducting $A_{x}B_{y}$ compound, e.g. V_{x} ...

Summary of the Invention:

...the humidity from 0 to 50% relative humidity. Sadaoka, Y.; Sakai, Y.; Murata, Y. U.; **Sensors** and Actuators 1993, B 13-14, 420-423 report a similar behavior of an optical **sensor** based on calcein-poly(acrylonitrile) in the case of **ammonia** detection. The sensitivity increased when I/I_0 (optical intensity ratio) decreased from 0.95...

...tector, DM 189) deposited on a mass-sensitive device (Boeker, P.; Horner, G.; Rosler, S. **Sensors** and Actuators 2000, B 70, 37-42). The response to 100 ppm **ammonia** (in Hertz) is double at 20.000 ppm water (saturated, humidity) compared to the response...

...main problem appears to be the size, which is in the centimeter scale. Metal oxide **sensors** can also detect **ammonia**, with a detection limit of about 25 ppm, but they suffer from their high power consumption and a...

...a substrate, a sensor medium formed on the substrate, the sensor medium comprising one-dimensional **nanoparticles**, wherein the one-dimensional **nanoparticles** essentially consist of a semiconducting $A_{x}B_{y}$ compound, wherein the semiconducting A...

...metal compounds have different selectivities towards a target analyte. The material of the one-dimensional **nanoparticles** used for assembling the sensor device are therefore selected depending on the analyte to be ...

...using e.g. V_{2O_5} as a material of the one-dimensional **nanoparticles** vanadium may be present in the V^{4+} as well as in the V^{5+} ...

...0027] The one-dimensional **nanoparticles** used as the sensitive medium in the sensor device according to the invention have a much larger extension in a longitudinal direction than in directions perpendicular thereto. Usually the **nanoparticles** have dimensions in the micrometer scale in a longitudinal direction and in the nanometer scale in both directions perpendicular thereto. Preferably the one-dimensional **nanoparticles** have a length of less than 100 μm , especially preferred less than...

...2, especially preferred less than 50 nm². The length of the

one-dimensional **nanoparticles** can conveniently be controlled by the reaction time during the synthesis of the one-dimensional **nanoparticles**. The one-dimensional **nanoparticles** have the shape of a fibre and therefore do not easily self-organize to form a close-packed arrangement as for example **nanoparticles** which have a spherical shape. Therefore voids within the sensor medium are increased allowing a...

...0028] The one-dimensional **nanoparticles** are present in the sensor medium as individual particles. It is sufficient to stabilize the sensor medium just by physical interactions and to deposit the one-dimensional **nanoparticles** on a substrate surface. To increase mechanical stability of the sensor medium the one-dimensional **nanoparticles** may be interlinked by e.g. bifunctional ligands or may be embedded in a matrix ...

...0029] The one-dimensional **nanoparticles** used in the sensor device according to the invention are made from a semiconducting material...

...A and B of the semiconducting $A_{\text{sub}}x B_{\text{sub}}y$ compound the one-dimensional **nanoparticles** have different selectivity towards a given analyte compared to the carbon-SWNT based sensors described by J. Kong et al. loc. cit. Methods for obtaining one-dimensional **nanoparticles**, as used in the sensor device according to the invention, are well established. The one-dimensional **nanoparticles** can easily be modified in their composition, e.g. by addition of a dopant, and...

...0031] The one-dimensional **nanoparticles** may be hollow or filled and may e.g. have the form of a nanotube or a nanowire. Filled one-dimensional **nanoparticles** are preferred. Further the one-dimensional **nanoparticles** may have various shapes of cross sections, e.g. may have a round (circular) or rectangular cross section. The one-dimensional **nanoparticles** may then have the form of a nanowire or a nanobelt. Nanobelts are especially preferred as sensing material. The sensor medium may also comprise bundles of one-dimensional **nanoparticles**.

[...]

...0032] The synthesis of one-dimensional **nanoparticles** formed of II-VI-semiconductors or III-V-semiconductors is e.g. described by X...

...P, examples for binary II-VI compounds are ZnS, ZnSe, CdS, and CdSe. One-dimensional **nanoparticles** have been prepared from the above-mentioned semiconducting materials in bulk quantities with high purity...

...0033] One-dimensional **nanoparticles** of semiconducting metal oxides can be prepared by a method described by Z. W. Pan...

...metal oxides that can be used as a source for the preparation of one-dimensional **nanoparticles** used in the sensor device according to the invention are e.g. $\text{Ga}_{\text{sub}20}$...

... $\text{sub}_{20}\text{sub}_{3}$, $\text{W}_{\text{sub}18}\text{sub}_{49}$, and $\text{GeO}_{\text{sub}2}$. One-dimensional **nanoparticles** consisting of semiconducting metal sulfides may be prepared from $\text{MoS}_{\text{sub}2}$, $\text{NbS}_{\text{sub}3}$...

... $\text{TiO}_{\text{sub}2}$ and $\text{SiO}_{\text{sub}2}$. The synthesis of $\text{Si}_{\text{sub}3}\text{N}_{\text{sub}4}$ -**nanoparticles** has been described by Han, W.; Fan, S.; Li, Q.; Hu, Y. Science 1997, 277...

...Levy, F.; Mihailovic, D. Science 2001, 292, 479-481 described the synthesis of one-dimensional **nanoparticles** made from GaSe...

...0035] One-dimensional **nanoparticles** can be prepared with a wide range of compounds using a porous template, e.g...

...via the appropriate technique, for example thermal decomposition or etching, leaving the required one-dimensional **nanoparticles**. Details towards the growth of one-dimensional **nanoparticles** are given e.g. in Caruso, R. A.; Schattka, J. H.; Greiner, A. Adv. Mat...

...or in combination with each other. For example it is possible to use one-dimensional **nanoparticles** made of pure $V_{20}S_5$. The physical characteristics of the one-dimensional...

...3, to the one-dimensional $V_{20}S_5$ -material. Further different one-dimensional **nanoparticles** made of different semiconducting materials may be used within a single sensor medium of the...

...according to the invention. The sensor medium then contains e.g. a first one-dimensional **nanoparticle** made of a first semiconducting A_xB_y compound and a second one-dimensional **nanoparticle** made of a second semiconducting A_xB_y compound...

...0037] Preferably the semiconducting one-dimensional **nanoparticles** are made of a vanadium oxide material. Vanadium pentoxide one-dimensional **nanoparticles** are easily obtained by wet-chemistry, in large amounts and as pure material. They can...

...0039] The one-dimensional **nanoparticles** can be employed as synthesized in an undoped form. To modify and to tune the...

...sensitivity of the sensors according to the invention towards a target analyte the one-dimensional **nanoparticles** may be doped with a dopant. Sensors with appropriate dopants are highly sensitive and allow...

...which are incorporated in the structure or immobilized at the surface of the one-dimensional **nanoparticle**. This is possible by exchanging protons at the surface of the one-dimensional **nanoparticle**. In case of vanadium oxide most of the vanadium atoms in the one-dimensional vanadium...

...V oxidation state hydroxy groups may be formed on the surface of the one-dimensional **nanoparticle** by partially hydrolysing the vanadium oxide in water. Such hydroxy groups are acidic and the...

...0041] The one-dimensional **nanoparticles** can also be doped by intercalation of neutral molecules between layers of the one-dimensional **nanoparticles**. This implies swelling of the structure inducing a weakening of the interaction forces between different layers of the one-dimensional **nanoparticle**. Such an intercalation of neutral molecules between layers of vanadium pentoxide xerogels is e.g...

...is also possible to immobilize molecules or particles on the surface of the one-dimensional **nanoparticle**.

[...]

...or nitrate salt may also be employed. Also possible is to dip the one-dimensional **nanoparticles** into a solution containing the metal which is used as a dopant in solid form. The metal is then oxidized and

incorporated into the one-dimensional **nanoparticles** . Such an incorporation of metal ions into vanadium pentoxide xerogels has been described e.g...

...0043] Further the one-dimensional **nanoparticles** can be doped with organic molecules. A broad variety of organic molecules may be used...

...and pyrrole derivatives. The organic molecules are adsorbed on the surface of the one-dimensional **nanoparticles** or intercalated between layers the one-dimensional **nanoparticles** thereby modifying the physical and chemical characteristics of the one-dimensional **nanoparticles** . For example T. Kuwahara, H. Tagaya and J. Kadokawa, Inorganic Chemistry Communications, 2001, 4, 63...

...S. D. Huang, Angewandte Chemie International Edition, 1999, 38, 1751-1754. Furthermore the one-dimensional **nanoparticles** can be doped with conducting polymers. Such inorganic-organic hybrid microstructures are known e.g...

...Furthermore also large organic cations can be incorporated into the structure of the one-dimensional **nanoparticles** . Such a material has been described. e.g. by M. Inagaki, T. Nakamura and A...

...0044] Also ion complexes can be used as a dopant for doping the one-dimensional **nanoparticles** . An ion complex that can be used as a dopant according to the invention are...

...of the invention the sensor medium of the chemical sensor device additionally comprises a second **nanoparticle** material which preferably has an approximately spherical shape. The incorporation of second **nanoparticles** different from the one-dimensional **nanoparticles** into the sensor medium allows the modification of the sensor selectivity and sensor sensitivity. Metal **nanoparticles** can be formed by evaporation of the metal on the one-dimensional **nanoparticles** pre-immobilized on the substrate. Further metal **nanoparticles** stabilized with an organic shell can be prepared e.g. by wet chemical methods. A method for preparing such **nanoparticles** is e.g. described by M. Brust, J. Fink, D. Bethell, D. J. Schiffrin and...

...Chem. Commun., 1995, 1655-1656. This technique is applicable to a wide range of metal **nanoparticles** . Examples are Fe, Au, Ag, Pt, Pd, as well as some binary **nanoparticles** , like Fe/Pt. Such stabilized **nanoparticles** are soluble in common organic solvents. These **nanoparticles** can be immobilized on the one-dimensional **nanoparticles** by simply dipping the substrate pre-coated with the one-dimensional **nanoparticles** in the corresponding solution of the second **nanoparticle** . A chemical coupling between the one-dimensional **nanoparticles** and the second **nanoparticles** is possible through a bi- or polyfunctional organic linker compound. Finally, certain metal ion complexes...

...doping vanadium pentoxide nanobelts with a metal e.g. gold. It can be doped with **nanoparticles** stabilized with an organic shell, or by evaporation of a thin metal layer or with a metal salt that is converted to **nanoparticles** during the doping process...

...0047] According to a preferred embodiment the second **nanoparticles** consists of a semiconducting material. As a semiconducting material may be used e.g. II...

...also be used as a mass sensitive sensor. The sensitive film comprising

the one-dimensional **nanoparticles** is then used as a coating on a piezo-electric material to form a chemically...

- ...luminescence properties may change when the analyte molecules are adsorbed to the semiconducting one-dimensional **nanoparticles**. This change is due to a change of the electronic states of the one-dimensional **nanoparticles** and/or of the close environment of the one-dimensional **nanoparticles**. Furthermore the one-dimensional **nanoparticles** can be combined with appropriate chemicals, e.g. dyes, to induce a change of optical...
- ...top of the sensor film. By the sorption of the analyte to the one-dimensional **nanoparticles** the electronic properties of the sensor are influenced resulting in a change of conductivity of...
- ...0060] The small size of the one-dimensional **nanoparticles** allows readily miniaturisation of the devices. The chemical sensor according to the invention therefore may...
- ...0061] The one-dimensional **nanoparticles** used in the chemical sensor device according to the invention have a quite high electrical conductivity. This is especially the case when vanadium pentoxide is used as the one-dimensional **nanoparticles**. Vanadium oxide comprises vanadium in the valence +IV and +V state and therefore already provides...
- ...into the structure of the sensing material. Depending on the length of the one-dimensional **nanoparticles** also sensor devices comprising a single one-dimensional **nanoparticle** may be prepared. In this case preferably a single one-dimensional **nanoparticle** is bridging the gap between the two electrodes. A single one-dimensional **nanoparticle** is sufficient to obtain a sensor medium but also several **nanoparticles** may be arranged in a more or less parallel arrangement. One-dimensional **nanoparticles** of smaller size than the gap size of the electrode pair may be arranged to form a network. The one-dimensional **nanoparticles** then form intersections at which the surface areas of neighboured **nanoparticles** are in contact with each other thereby providing a conductive path between the electrodes. The...
- ...00066] b) providing one-dimensional **nanoparticles** essentially consisting of a semiconducting $A_{\text{sub}}x B_{\text{sub}}y$ compound, wherein A, B, x
...
- ...00067] c) coating the substrate surface with the one-dimensional **nanoparticles** thereby obtaining a sensor medium...
- ...0069] The one-dimensional **nanoparticles** can be prepared by known methods. An overview on methods for obtaining one-dimensional vanadium synthesis conditions. The addition of a surfactant during the preparation of the one-dimensional **nanoparticles** introduces a high porosity as has been shown for vanadium alkoxide derived gels by S...
- ...0070] The one-dimensional **nanoparticles** can be deposited on the substrate by spin-coating, drop-coating, dip-coating, brush techniques...
- ...0071] The one-dimensional **nanoparticles** can be aligned during deposition e.g. to bridge two chemiresistor electrodes. Alignment of one-dimensional **nanoparticles** is preferred when using only few **nanoparticles** to form a sensor medium, and allows a high reproducibility of the fabrication process. Alignment of the one-dimensional **nanoparticles** may be achieved by MIMIC (Micro Moulding in Capillaries) technique described by H. J. Muhr...

...0075] When using vanadium pentoxide nanofibres as a one-dimensional **nanoparticles** the chemical sensor device is sensitive to gases, say CO, H₂, NH₃ but also to SO_x, O₂ or NO_x. The **sensor** is highly sensitive to **ammonia** and polar organic molecules, like amines or thiols and **detection** below 0,5 ppm is possible. By changing the dopant, it is possible to create **sensors** with the same starting material, which cover the whole range of concentration for a given...

...detection of amines. It could be demonstrated by the inventors that it is possible to **detect** amines in low concentrations down to 30 ppb at high humidity. Biogenic amines are often encountered in fermented foodstuff. For example, trimethylamine or **ammonia** is produced during fish decomposition. Therefore volatile amines may be used as indicator of fish...

...can also be diagnosed by a specific pattern of volatile amines in urine. In addition, **ammonia** is often used in the chemical industry and the **detection** method according to the invention may be used to **detect** leaks...

...0085] FIG. 2 schematically displays different types for the arrangement of one-dimensional **nanoparticles** to bridge a gap between a pair of electrodes...

Description of the Invention:

[0096] FIG. 1 schematically shows a chemiresistor, which has a sensor medium comprising one-dimensional **nanoparticles** (nanobelts) as a sensitive material. On a substrate 1 are placed interdigitated electrodes 2. The electrode structures 2 are covered by a sensor film, which is formed of one-dimensional **nanoparticles** 3. A constant current may be applied to the leads of the electrodes 2 and...

...0097] FIG. 2 displays different arrangements of one-dimensional **nanoparticles** 4 between a pair of electrodes 2. In FIG. 2a a single one-dimensional **nanoparticle** 4 is bridging the gap between the pair of electrodes 2. For simplicity only one one-dimensional **nanoparticle** is shown on the figure. Several particles can also be employed. In this arrangement, the analyte can modulate the conductivity along the one-dimensional **nanoparticle** by adsorption on its surface and/or by intercalation. The analyte can also influence the...

...with the particles changing the intrinsic conductivity of the one-dimensional particles. The one-dimensional **nanoparticles** can have a length much smaller than the gap size between a pair of electrodes. The one-dimensional **nanoparticles** are then arranged in a random order to form a network of **nanoparticles** 4 between a pair of electrodes 2 as shown in FIG. 2b. Like in the...

...the interparticle contacts. In this arrangement the analyte enhances or reduces the conduction between the **nanoparticles**. The arrangement shown in FIG. 2b is preferred when the analyte interacts with the interparticle contacts. Between individual one-dimensional **nanoparticles** 4 are formed voids, which provide an easy access of the analyte to the **nanoparticle** surface even when a sensor medium of a larger thickness is used...

...0105] The one-dimensional **nanoparticles** were deposited onto BK7 glass substrates supporting lithographically made interdigitated electrode structures. The electrode structures...

...0107] The fabrication procedure described under (c) was repeated but as

one-dimensional **nanoparticles** were used silver doped vanadium pentoxide nanofibres obtained under (b). Thereby a silver doped V...

...0115] The responses of **sensors** 1-3 are also graphically displayed in FIG. 3. Whereas **sensors** 1 and 2 have about the same sensitivity to **ammonia** (in absolute value), **sensor** 2 has a sensitivity towards CO which is about 5 times larger than for **sensor** 1. By combining these two **sensors** it is therefore possible to distinguish NH_3 and CO. **Sensor** 3 is less sensitive to **ammonia** than **sensors** 1 and 2, but is more sensitive to H_2 . This makes this **sensor** more suitable for applications where **detection** of hydrogen is required...

...0119] **Sensor** 7 was exposed to 360 ppb **ammonia**. The response of the **sensor** is displayed in FIG. 6. The **sensor** displayed a fast response of $\Delta R/R_{\text{ini}} - 1.6\%$ within 120 seconds. This demonstrates that the **sensor** is sensitive to very low concentrations of **ammonia** giving a fast response and a short recovery period. At higher **ammonia** concentrations an increased response of the **sensor** is obtained as is obvious from the sensitivity isotherm displayed in FIG. 7...

Exemplary or Independent Claim(s):

...a substrate, a sensor medium formed on the substrate, the sensor medium comprising one-dimensional **nanoparticles**, wherein the one-dimensional **nanoparticles** essentially consist of a semiconducting A_xB_y compound, wherein the semiconducting A ...

Non-exemplary or Dependent Claim(s):

- ...7. Chemical sensor device according to claim 1, wherein the one-dimensional **nanoparticles** are filled...
- ...8. Chemical sensor device according to claim 1, wherein the one-dimensional **nanoparticles** have a rectangular cross section...
- ...9. Chemical sensor device according to claim 1, wherein the one-dimensional **nanoparticles** are provided in the form of a bundle ...
- ...10. Chemical sensor device according to claim 1, wherein the one-dimensional **nanoparticle** further comprises a dopant...
- ...sensor device according to claim 10, wherein the dopant is intercalated within the one-dimensional **nanoparticle** and/or is adsorbed on the surface of the one-dimensional **nanoparticle** .
- ...
- ...15. Chemical sensor device according to claim 1, wherein the sensor medium additionally comprises second **nanoparticles** different from the one-dimensional **nanoparticles** .
- ...
- ...16. Chemical sensor according to claim 15, wherein the second **nanoparticles** have an approximately spherical shape...
- ...17. Chemical sensor device according to claim 15, wherein the second **nanoparticle** essentially consists of a metal...
- ...claim 1, wherein the sensor material comprises at least 1 individual of said one-dimensional **nanoparticles** bridging a gap between two electrodes provided on the substrate...

...the following steps:

- a) providing a substrate having a substrate surface;
- b) providing one-dimensional **nanoparticles** essentially consisting of a semiconducting A_xB_y compound as defined in claim 1;
- c) coating the substrate surface with the one-dimensional **nanoparticles** thereby obtaining a sensor medium;
- d) providing detection means for detecting a change of a...

...24. Method according to claim 23, wherein the one-dimensional **nanoparticles** are aligned on the substrate surface...

...25. Method according to claim 23, wherein the one-dimensional **nanoparticles** are fixed to the substrate surface by a bifunctional ligand which is linked to the substrate surface by a first functional group and to the one-dimensional **nanoparticle** surface by a second functional group

4/3,KWIC/48 (Item 13 from file: 654)
DIALOG(R) File 654:US Pat.Full.
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5993665

Derwent Accession: 2005-180389

UTILITY

Combined nanotechnology and sensor technologies for simultaneous diagnosis and treatment

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Main Patent	US 20050037374	A1	20050217	US 2003744789	20031223
CIP	PENDING			US 2003345532	20030116
CIP	PENDING			US 2002274829	20021021
CIP	PENDING			US 2002154201	20020522
CIP	ABANDONED			US 2000708789	20001108
Provisional				US 60-292962	20010523
Provisional				US 60-164250	19991108

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Abstract:

...and methods for diagnosing and/or treating conditions, diseases, or disorders. The present invention uses **nanoparticle** -based assemblies, which comprise a **nanoparticle** ; a surrogate marker; and a means for detecting a specific chemical entity. Such **nanoparticle** -based assemblies combine nanotechnology and sensor technology to provide an efficient and accurate means for...

Summary of the Invention:

...biosensors), and the identification of biomarkers for specific diseases and/or conditions. Nanotechnology, such as **nanoparticles** , offers many advantages when used for applications such as the delivery of

bioactive agents (i...

...gene therapy, immunosuppressants, chemotherapeutics), and drug uptake and degradation (i.e., enzyme encapsulation). For example, **nanoparticles** have been proposed as providing site-specific distribution of drugs to a target site. Appropriately...

...a patient. This invention is based in part on nanostructure-based assemblies that include: a **nanoparticle** ; a means for detecting an SCE; and a means for notifying the physician or healthcare...

...assembly of the invention. The nanostructure-based assembly of the invention is composed of a **nanoparticle** that contains the following components: (a) a means for detecting an SCE; and (b) a surrogate marker. In another embodiment, the **nanoparticle** contains an additional component, (c) a "payload." These components can be attached to any surface of the **nanoparticle** .
[...]

...SCE by the SCE-detecting means affects the release of the surrogate marker from the **nanoparticle** . Because the surrogate marker is released from the **nanoparticle** only in the presence of an SCE, detection of the surrogate marker provides notice that...

...0027] In one embodiment, the **nanoparticle** -based assemblies of the invention are composed of biodegradable substances. In another embodiment, the **nanoparticle** -based assemblies are composed of biocompatible substances...

...0028] In another embodiment of the present invention, the **nanoparticle** of the nanostructure-based assembly has a hollow body defining an inner void, which contains...

...undergo a conformational change upon detecting the SCE to detach the end-cap from the **nanoparticle** and release both the surrogate marker and the payload. In certain embodiments, the **nanoparticle** contains only the surrogate marker...

...In a related embodiment, the detecting means is attached to the outer surface of the **nanoparticle** . The controlled release of the surrogate marker and, when present, payload is accomplished by the release of the end-cap, which is attached to the **nanoparticle** via chemically labile bonds...

...0030] Yet another embodiment provides a **nanoparticle** that has the detecting means, the surrogate marker, and the payload (when present) applied to the outside of the surface of the **nanoparticle** . All of these components are attached to the surface of the **nanoparticle** via chemically labile bonds, which allow for the release of these components under specific conditions

Description of the Invention:

...1 is a table illustrating certain specific chemical compounds that can be detected using the **nanoparticle** -based assemblies of the present invention...

...disorder. The systems and methods of the invention utilize nanostructure-based assemblies that contain a **nanoparticle** , a means for detecting a target SCE, and a surrogate marker. In certain embodiments, nanostructure...

...and the target SCE induces the release of the surrogate marker and payload from the **nanoparticle**. Advantageously, the concentration of the released surrogate marker is proportional to the amount of SCE...

...0056] **Nanoparticles**

[...]

...detection, notification, and treatment of a condition, disorder, or disease. Such assemblies are based on **nanoparticles**, which provide a mechanism for the targeted delivery and release of detectable markers and/or...

...0058] According to the present invention, **nanoparticles** can be produced in a wide range of sizes and shapes, and composed of a...

...limited to, spherical, elliptical, cubic, cylindrical, tetrahedron, polyhedral, irregular-prismatic, icosahedral, and cubo-octahedral forms. **Nanoparticles** intended for in-vivo use are of any dimension, preferably with a maximum dimension less...

...proper distribution at the microvasculature level, without any occlusion of blood flow. More preferably, the **nanoparticles** of the subject invention are of a dimension less than 100-150 nm. The "maximum dimension" of a **nanoparticles** is the maximum distance between any two points in the **nanoparticle**. In a preferred embodiment, the **nanoparticles** are in the form of tubular bodies (also known as "nanotubes"), which are either hollow...

...0059] Methods of preparation of **nanoparticles** are well known in the art. For example, the preparation of monodisperse sol-gel silica...

...0060] **Nanoparticles**, in accordance with the present invention, can be prepared from a single material or a...

...materials including, but not limited to, polymers, semiconductors, carbons, or Li^[sup]+ intercalation materials. Metal **nanoparticles** include those made from gold or silver. Semi-conductor **nanoparticles** include those made from silicon or germanium. Polymer **nanoparticles** include those made from biocompatible or biodegradable polymers. The ability to make **nanoparticles** from a wide variety of materials or combination of materials allows the creation of **nanoparticles** with desired biochemical properties such as biocompatibility, including immunogenic compatibility, and/or, biodegradability. In comparison...

...0061] **Nanoparticles** of the present invention can be synthesized using a template synthesis method. For example, **nanoparticles** can be synthesized using templates prepared from glass (Tonucci, R. J. et al., Science 258...

...and a variety of other materials (Ozin, G. A., Adv. Mater., 4, 612 1992)). Alternatively, **nanoparticles** can be prepared using a self-assembly process, as described in Wang, Z. L., "Structural...

...0062] In one embodiment, a nanostructure-based assembly of the invention contains a **nanoparticle**, which has one or more surfaces functionalized to allow attachment of SCE-detectors to the surface. Such "functionalized" **nanoparticles** have at least one surface modified to allow for directed (also referred to as "vectoring") delivery and/or controlled release of the payload and surrogate marker. In certain embodiments, the **nanoparticle** is formed with an interior void.

Different chemical and/or biochemical functional groups can be applied to the inside and/or outside surfaces of the **nanoparticle** to enable the attachment of an SCE-detector, surrogate marker, and/or payload on a **nanoparticle** surface...

...0063] In another embodiment, the nanostructure-based assembly contains a **nanoparticle** formed with an interior void to contain a surrogate marker, a payload, and a detachable...

...presence of a target SCE, the SCE-detector mechanically detaches the end-cap from the **nanoparticle** to release the surrogate marker for analysis by sensor technology. Simultaneously, the payload is released...

...0064] In a preferred embodiment, the **nanoparticle** is in the form of a nanotube that is hollow and has a first open...

...the end-cap, the surrogate marker and payload are released with the uncapping of the **nanoparticle**. The uncapping mechanism may require the use of energy-bearing biomolecular motors such as, but...

...filament elongation model for actin-based motors," Biophys J, 82:605-617 (2002)). Once the **nanoparticle** is uncapped, the released surrogate marker can then be detected using sensor technology known in...

...0067] A number of patents and publications describe **nanoparticles** in the form of tubes (nanotubes). For example, U.S. Pat. No. 5,482,601... substrate aluminum surface (Hornyak, G. L., et al., "Fabrication, Characterization and Optical Properties of Gold- **Nanoparticle** /Porous-Alumina Composites: The Non-Scattering Maxwell-Garnett Limit," J. Phys. Chem. B., 101:1548...

...0073] Suitable end-caps used to block a nanotube opening include, for example, **nanoparticles** having a diameter slightly larger than the inside diameter of the **nanoparticle** so as to occlude the open end of the **nanoparticle**. End-caps are any piece of matter and can be composed of materials that are chemically or physically similar (or dissimilar) to the **nanoparticle**. The end-cap can be a particle that has a maximum dimension of less than...

...sub]2) [sub]3-SH could be attached to a silica nanotube and a gold **nanoparticle** attached as the end-cap using the -SH end of this molecule. It is well...

...0078] Contemplated end-caps for the invention include **nanoparticles** that can be electrophoretically placed within the mouths of nanotubes so that the entire mouth of the nanotube is blocked when disulfide bonds are formed between the nanotube and the **nanoparticle** as described in Miller, S. A. and C. R. Martin, "Electroosmotic Flow in Carbon Nanotube ...

...caps can be suspended in solution together with the activated disulfide labeled nanotubes. Here, the **nanoparticle** caps can spontaneously self-assemble to the nanotubes. The self-assembly of gold nanospheres and ...

...1202-1205 (1999)), and antigen/antibody interactions (Shenton, W. et al., "Directed Self-Assembly of **Nanoparticles** into Macroscopic Materials Using Antibody-Antigen Recognition," Adv. Mater., 11:449 (1999 ...

...e., surrogate marker and/or payload material). Methods for attaching an

end-cap to a **nanoparticle** include, but are not limited to, using: electrostatic attraction, hydrogen bonding, acid and/or basic sites located on the end-cap/ **nanoparticle** , covalent bonds, and other chemical linkages...

...affect the release of the surrogate marker and/or payload material via uncapping of the **nanoparticle** . For example, the uncapping mechanism is based upon the detection by the detecting means of...

...0093] Functionalization of the **Nanoparticles**
[...]

...0094] According to the present invention, **nanoparticles** can be prepared having different chemically or biochemically functionalized surfaces to enable attachment of an SCE-detecting means, surrogate marker, and/or payload. Methods used to functionalize a **nanoparticle** surface depend on the composition of the **nanoparticle** and are well known in the art. For example, functionalization of silica **nanoparticles** is accomplished using silane chemistry. With silane chemistry, different functional groups can be attached to the surfaces of the **nanoparticle** by attaching a functional group to the **nanoparticle** surface while the **nanoparticles** are embedded within the pores of the template. Then, a hydrolytically unstable silane is reacted with the surface silanol sites on the **nanoparticle** to obtain covalent oxygen/silicon bonds between the surface and the silane. Additional functional groups can also be attached to the **nanoparticle** surface after dissolution of the template...

...0095] The surface of polymer **nanoparticles** can also be functionalized using well known chemical methods. For example, methods employed for polylactide...

...groups to enable attachment of a detecting means, surrogate marker, and/or payload to a **nanoparticle** surface...

...standard methods and used for random copolymerization with lactide. In accordance with the present invention, **nanoparticles** can have functional groups on any surface to enable the attachment of an SCE-detecting...

...peptides, RNA or DNA aptamers, cellular reporters or cellular ligands, can be attached to a **nanoparticle** surface to provide a means for vectoring the nanostructure-based assembly to a target SCE...

...covalently, including attachment via linker molecules. SCE-detecting means can also be attached to a **nanoparticle** surface by non-covalent linkage, for example, by absorption via hydrophobic binding or Van der...

...In addition, the detecting means, surrogate marker, and/or payload can be incorporated into the **nanoparticle** framework, which can include chitosan, PEGylated PLGA (poly(lactic-co-glycolic acid), or other PEGylated...

...PEG-maleimide can be incorporated into chain-end thiols on the outer surface of the **nanoparticles** . Alternatively, the detecting means, surrogate marker, and/or payload can be incorporated into **nanoparticle** frameworks composed of biodegradable and/or resorbable materials including, for example, polylactide based polymers as...

...0099] For **nanoparticles** comprising a hollow void in which the surrogate marker can be contained, a surrogate marker...

...Flow in Carbon Nanotube Membranes," J. Am. Chem. Soc., 123(49):12335-12342 (2001)). Alternatively, **nanoparticles** embedded within the synthesis membrane can be filled with a surrogate marker by vacuum filtering...

...the synthesis membrane. (See Parthasarathy, R. and C. R. Martin, Nature, 369:298 (1994)). For **nanoparticles** prepared by formation within an alumina template film prior to removal of the alumina from...

...0107] A nanostructure-based assembly of the invention comprises a **nanoparticle**, which contains a means for detecting a target SCE, a surrogate marker, and a payload...

...proteins. Such aptamer-linked proteins can then be immobilized on a functionalized surface of a **nanoparticle**. For example, aptamer-linked proteins can be attached covalently to a **nanoparticle** end-cap or to an exterior **nanoparticle** surface, including attachment of the aptamer-linked protein by functionalization of the surface. Alternatively, aptamer-linked proteins can be covalently attached to a **nanoparticle** surface via linker molecules. Non-covalent linkage provides another method for introducing aptamer-linked proteins to a **nanoparticle** surface. For example, an aptamer-linked protein may be attached to an **nanoparticle** surface by absorption via hydrophilic binding or Van der Waals forces, hydrogen bonding, acid/base...

...0116] By way of example, one embodiment of the present invention uses **nanoparticle**-based sensors that contain anti-oxidant genes (MnSOD, HO-1, and PON1), which are released...0148] In one embodiment, a patient suffering from heroin addiction is administered a composition comprising **nanoparticle**-based assemblies of the invention. The **nanoparticle**-based assemblies are designed to detect the drug heroin. In one embodiment, the **nanoparticle**-based assemblies contain a **nanoparticle**, a surrogate marker, and an SCE-detector. Preferably, the SCE-detector is an aptamer that...

...aptamer and the surrogate marker (heroin-surrogate marker) are attached to a surface of the **nanoparticle**.
[...]

...a preferred embodiment, the heroin-aptamer is attached to an end-cap of a hollow **nanoparticle** that contains therein the heroin-surrogate marker. The heroin-aptamer is designed so that upon interaction with heroin, the end-cap is released from the **nanoparticle** to release the heroin-surrogate marker. The heroin-surrogate marker is readily detectable in bodily...

...0150] To test for heroin use, the **nanoparticle**-based assemblies are administered to the patient and then a sample of the patient's...

...is present in the patient, the heroin interacts with the heroin-aptamer and "uncaps" the **nanoparticle**, thus releasing the heroin-surrogate marker for identification in the bodily fluid sample. Any one...

...another embodiment of the invention, a patient suffering from atherosclerosis is administered a composition comprising **nanoparticle**-based assemblies to diagnose and treat atherosclerosis. The **nanoparticle**-based assembly comprises a **nanoparticle**; a surrogate marker; a payload; and an SCE-detector. Treatment of atherosclerosis (payload) comprises anti...

...0153] Glycogen is readily detectable in bodily fluids (i.e., blood) using a **nanoparticle** -based assembly of the invention. According to the present invention, the **nanoparticle** -based assembly comprises a **nanoparticle** , a surrogate marker, and an SCE-detector that is designed to bind to the glycogen

Exemplary or Independent Claim(s):

...disease, or disorder, comprising:

- (a) administering to a patient a composition comprising at least one **nanoparticle** -based assembly, wherein the **nanoparticle** -based assembly comprises a **nanoparticle** ; a surrogate marker, and a means for detecting a specific chemical entity (SCE);
- (b) obtaining...

...disease, or disorder, comprising:

- (a) administering to a patient a composition comprising at least one **nanoparticle** -based assembly, wherein the **nanoparticle** -based assembly comprises a **nanoparticle** ; a surrogate marker, a means for detecting a specific chemical entity (SCE), and a payload...

Non-exemplary or Dependent Claim(s):

2. The method according to claim 1, wherein the **nanoparticle** is a nanotube...

...8. The method according to claim 1, wherein the SCE- detecting means has a specific action on compounds selected from the group consisting of acetaldehyde, acetone, ammonia , carbon monoxide, chloroform, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, O-toluidine, pentane sulfides and sulfides, H...

...11. The method according to claim 1, wherein the **nanoparticle** is formed with an interior void that contains the surrogate marker, wherein the **nanoparticle** has at least one open end to provide access to the interior void...

...13. The method according to claim 11, wherein the **nanoparticles** further includes an end-cap to block the open end...

...15. The method according to claim 13, wherein the end-cap is attached to the **nanoparticle** by covalent bonds...

...16. The method according to claim 13, wherein the **nanoparticle** is in the form of a tubular body; and wherein the SCE-detecting means is...

...17. The method according to claim 1, wherein the **nanoparticle** is composed of silica...

...18. The method according to claim 1, wherein the **nanoparticle** is composed of a polymer...

...to claim 18, wherein the SCE-detecting means is attached to a surface of the **nanoparticle** using copolymerization...

...20. The method according to claim 18, wherein the polymer **nanoparticle** is composed of polymers selected from the group consisting of polystyrene, polyorganosiloxane, poly(methyl methacrylate)...

...21. The method according to claim 18, wherein the polymer **nanoparticle** is composed of biodegradable polymers selected from the group consisting of poly(caprolactone), poly(glycolic)...

- ...22. The method according to claim 18, wherein the polymer nanoparticle is composed of biocompatible polymers selected from the group consisting of poly(lactide-co-glycolide)...
- ...The method according to claim 1, wherein the SCE-detecting means is incorporated into the nanoparticle .
...
- ...24. The method according to claim 1, wherein the nanoparticle is produced in a shape selected from a group consisting of spherical; elliptical; cubic; cylindrical...
- ...25. The method according to claim 1, wherein the nanoparticle has a dimension less than 500 nm...
- ...26. The method according to claim 1, wherein the surface of the nanoparticle is stealthy...
- ...28. The method according to claim 27, wherein the nanoparticle is a nanotube...
- ...34. The method according to claim 27, wherein the SCE- detecting means has a specific action on compounds selected from the group consisting of acetaldehyde, acetone, ammonia , carbon monoxide, chloroform, diethylamine, hydrogen, isoprene, methanethiol, methylethylketone, O-toluidine, pentane sulfides and sulfides, H...
- ...37. The method according to claim 27, wherein the nanoparticle is formed with an interior void that contains the surrogate marker, wherein the nanoparticle has at least one open end to provide access to the interior void...
- ...39. The method according to claim 37, wherein the nanoparticles further includes an end-cap to block the open end...
- ...41. The method according to claim 39, wherein the end-cap is attached to the nanoparticle by covalent bonds...
- ...42. The method according to claim 39, wherein the nanoparticle is in the form of a tubular body; and wherein the SCE-detecting means is...
- ...43. The method according to claim 27, wherein the nanoparticle is composed of silica...
- ...44. The method according to claim 27, wherein the nanoparticle is composed of a polymer...
- ...to claim 44, wherein the SCE-detecting means is attached to a surface of the nanoparticle using copolymerization...
- ...46. The method according to claim 44, wherein the polymer nanoparticle is composed of polymers selected from the group consisting of polystyrene, polyorganosiloxane, poly(methyl methacrylate)...
- ...47. The method according to claim 44, wherein the polymer nanoparticle is composed of biodegradable polymers selected from the group consisting of poly(caprolactone), poly(glycolic)...
- ...48. The method according to claim 44, wherein the polymer nanoparticle is composed of biocompatible polymers selected from the group consisting of poly(lactide-co-glycolide)...

...The method according to claim 27, wherein the SCE-detecting means is incorporated into the nanoparticle .

...

...50. The method according to claim 27, wherein the nanoparticle is produced in a shape selected from a group consisting of spherical; elliptical; cubic; cylindrical...

...51. The method according to claim 27, wherein the nanoparticle has a dimension less than 500 nm...

...52. The method according to claim 27, wherein the surface of the nanoparticle is stealthy

4/3,KWIC/49 (Item 14 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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5970135 **IMAGE Available

Derwent Accession: 2004-642005

UTILITY

REASSIGNED

Inorganic dopants, inks and related nanotechnology

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Examiner: Le, H. Thi

Legal Representative: Hogan & Hartson LLP; Langley, Stuart T.

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6849109	B2	20050201	US 2003455874	20030606
Related Publ	US 20040170820	A1	20040902		
Division	US 6602595	A		US 2002150722	20020517
Division	US 6344271	A		US 99274517	19990323
Division	PENDING			US 455874	
Division	PENDING			US 2001790036	20010220
Division	US 6228904	A		US 9883893	19980522
Division	US 6202471	A		US 9874534	19980507
CIP	US 5905000	A		US 96739257	19961030
CIP	US 5952040	A		US 96730661	19961011
CIP	US 5851507	A		US 96706819	19960903
CIP	US 5788738	A		US 96707341	19960903
CIP	PENDING			US 455874	
CIP	US 6513362	A		US 2001753806	20010103
Provisional				US 60-111442	19981208
Provisional				US 60-107318	19981106
Provisional				US 60-79225	19980324
Provisional				US 60-69936	19971217
Provisional				US 60-49077	19970609

US Term Extension: 115 days

Fulltext Word Count: 25946

Summary of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle . A polymer coating may further be used to enable

selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle .

[...]

...00108] A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...00109] In some examples of biomedical functions, magnetic non-stoichiometric nanoparticles such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric nanoparticles can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric nanoparticles can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric nanoparticulate fillers are anticipated to have utility for chemotherapy. Nanoparticles suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic nanoparticles may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric nanoparticulate fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that nanoparticulates can be released into the body in a controlled fashion over a long time period...

...composition or with a phase that is compatible with the matrix composition. Such a coated nanoparticle is illustrated in FIG. 1, which shows a spherical nanoparticle 6 and a coating 8. In one embodiment, when embedding nanofillers in a polymer matrix...

...the filler may also be utilized as a means to time drug-release from a nanoparticle . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle .

[...]

...00139] A nanoparticulate filler for biomedical operations might be a carrier or support for a drug of interest...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites may also have utility as markers or as carriers for markers. Their unique...

...00140] In some examples of biomedical functions, magnetic nanoparticles such as ferrites may be utilized to carry drugs to a region of interest,

where the particles may then be concentrated using a magnetic field. Photocatalytic **nanoparticles** can be utilized to carry drugs to region of interest and then photoactivated. Thermally sensitive **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive **nanoparticulate** fillers may have utility for chemotherapy. **Nanoparticles** suitably doped with genetic and culture material may be utilized in similar way to deliver...

...in concentrating the particle and then providing the therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest using magnetic field, and finally activated using photons in the concentrated area. As markers, **nanoparticulate** fillers-coated or uncoated may be used for diagnosis of medical conditions. For example, fillers...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...by normal kidney action without the development of stones or other adverse side effects. While **nanoparticulates** may be removed naturally through kidney and other organs, they may also be filtered or removed externally through membranes or otherwise removed directly from blood or tissue. Carrier **nanoparticulates** may be reactivated externally through membranes and reused; for example, nutrient carriers may be removed... partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed...

4/3,KWIC/50 (Item 15 from file: 654)

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0005914605 **IMAGE Available

Derwent Accession: 2005-038668

Analyte detection in liquids with carbon nanotube field effect transistor devices

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Main Patent	US 20040253741	A1	20041216	US 2004773631	20040206
Provisional				US 60-445654	20030206

Fulltext Word Count: 4267

Summary of the Invention:

...for example, to be sensitive to the presence of various gases, such as oxygen and ammonia, and thus nanotubes included in an electrical circuit can operate as sensitive chemical sensors. NTFET devices, as

well as nanowire-based devices, are promising candidates for the electronic detection...

Description of the Invention:

...sensing of dissolved analytes. NTFETs were fabricated using nanotubes grown by chemical vapor deposition. Iron **nanoparticles** encased in mesoporous material were spin-coated and patterned on silicon substrates with 200 nm...

4/3,KWIC/51 (Item 16 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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5909631 **IMAGE Available

Derwent Accession: 2004-212649

Utility

Inorganic colors and related nanotechnology

Inventor: Yadav, Tapes, Longmont, CO

Assignee: NanoProducts Corporation(02), Longmont, CO

Examiner: Thile, H. (Art Unit: 173)

Combined Principal Attorneys: Langley, Stuart T.Hogan & Hartson LLP

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Main Patent	US 6830822	A	20041214	US 2003449278	20030530
Division	US 6602595	A		US 2002150722	20020517
Division	US 6344271	A		US 99274517	19990323
Division	Pending			US 2001790036	20010220
Division	US 6228904	A		US 9883893	19980522
Division	US 6202471	A		US 9874534	19980507
CIP	US 5905000	A		US 96739257	19961030
CIP	US 5952040	A		US 96730661	19961011
CIP	US 5851507	A		US 96706819	19960903
CIP	US 5788738	A		US 96707341	19960903
CIP	US 6513362	A		US 2001753806	20010103
	Pending			US 449278	

Fulltext Word Count: 26586

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

...

...A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be

utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...composition or with a phase that is compatible with the matrix composition. Such a coated **nanoparticle** is illustrated in FIG. 1, which shows a spherical **nanoparticle** 6 and a coating 8. In one embodiment, when embedding nanofillers in a polymer matrix...

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

...

...A **nanoparticulate** filler for biomedical operations might be a carrier or support for a drug of interest...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites may also have utility as markers or as carriers for markers. Their unique...

...In some examples of biomedical functions, magnetic **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic **nanoparticles** can be utilized to carry drugs to region of interest and then photoactivated. Thermally sensitive **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive **nanoparticulate** fillers may have utility for chemotherapy. **Nanoparticles** suitably doped with genetic and culture material may be utilized in similar way to deliver...

...in concentrating the particle and then providing the therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest using magnetic field, and finally activated using photons in the concentrated area. As markers, **nanoparticulate** fillers--coated or uncoated--may be used for diagnosis of medical conditions. For example, fillers...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...by normal kidney action without the development of stones or other adverse side effects. While **nanoparticulates** may be removed naturally through kidney and other organs, they may also be filtered or removed externally through membranes or otherwise removed directly from blood or tissue. Carrier **nanoparticulates** may be reactivated externally through membranes and reused; for example, nutrient carriers may be removed...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed...

4/3,KWIC/52 (Item 17 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005835471

Derwent Accession: 2004-756720

Chemical and biological agent sensor array detectors

Inventor: Steinthal, Gregory, INV

Sunshine, Steven, INV

Burch, Tim, INV

Plotkin, Neil, INV

Hsiung, Chang-Meng, INV

Assignee: Cyrano Sciences Inc.(02), Pasadena, CA, 91107

Smiths Detection - Pasadena, Inc.(02)

Correspondence Address: FOLEY AND LARDNER SUITE 500, 3000 K STREET NW,
WASHINGTON, DC, 20007, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20040204915	A1	20041014	US 2003698042	20031029
CIP	PENDING			US 2003624194	20030721
Provisional				US 60-397135	20020719
Provisional				US 60-422301	20021029

Fulltext Word Count: 17874

Description of the Invention:

...of superior chemical sensing performance properties relative to most previously available systems. Sensing materials include **nanoparticle** composite sensors such as polymer composite sensors, sensors based on nanotubes, and sol-gel based...surface-modified colloidal metal particle sensors other than carbon black. These include surface-modified gold **nanoparticles** as chemical sensors similar to the surface-modified carbon blacks described above. Use of these...

...a monolayer on the metal surface. In the present invention, both traditional polymer modified gold **nanoparticles** and biopolymer modified gold **nanoparticles** may be used as resistance based chemical and biological sensors. The resistive read out provides...

...vapor based on the array pattern. The C320 has been successfully tested as a point **detector** for TICs (e.g., hydrazine, **ammonia**, formaldehyde, ethylene oxide, insecticides) as well as CWAs (e.g., GA, GB, HN-3, VX... formulations, such as formulations of surface-modified carbon black

sensors, intrinsically conducting sensors, surface-modified nanoparticle metal sensors, and nanotube based sensors for ink jetting. Once a formulation exists, physical deposition...

...ink jetting candidates. Other useful ink-jetting materials and jettable formulations include surface modified gold nanoparticle formulations and nanotube formulations. Such formulations preferably have solid to solvent ratios in the range...

4/3,KWIC/53 (Item 18 from file: 654)
DIALOG(R) File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005797398 **IMAGE Available
Derwent Accession: 2004-688688
Nanomaterial compositions with distinctive shape and morphology
Inventor: Yadav, Tapesh, INV
Kosteletzky, Clayton, INV
Correspondence Address: HOGAN & HARTSON LLP, ONE TABOR CENTER, SUITE
1500 1200 SEVENTEENTH ST, DENVER, CO, 80202, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040180203	A1	20040916	US 2004811628	20040329
Division	US 6602595			US 2002150722	20020517
Division	US 6344271			US 99274517	19990323
Division	US 6228904			US 9883893	19980522
Continuation	PENDING			US 2003449278	20030530
CIP	PENDING			US 2001790036	20010220
CIP	US 5905000			US 96739257	19961030
CIP	US 5952040			US 96730661	19961011
CIP	US 5851507			US 96706819	19960903
CIP	US 5788738			US 96707341	19960903
Provisional				US 60-107318	19981106
Provisional				US 60-111442	19981208
Provisional				US 60-49077	19970609
Provisional				US 60-69936	19971217
Provisional				US 60-79225	19980324

Fulltext Word Count: 33436

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle .

[...]

...0107] A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0108] In some examples of biomedical functions, magnetic

non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...composition or with a phase that is compatible with the matrix composition. Such a coated **nanoparticle** is illustrated in FIG. 1, which shows a spherical **nanoparticle** 6 and a coating 8. In one embodiment, when embedding nanofillers in a polymer matrix...

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0142] A **nanoparticulate** filler for biomedical operations might be a carrier or support for a drug of interest...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites may also have utility as markers or as carriers for markers. Their unique...

...0143] In some examples of biomedical functions, magnetic **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic **nanoparticles** can be utilized to carry drugs to region of interest and then photoactivated. Thermally sensitive **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive **nanoparticulate** fillers may have utility for chemotherapy. **Nanoparticles** suitably doped with genetic and culture material may be utilized in similar way to deliver...

...in concentrating the particle and then providing the therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest using magnetic field, and finally activated using photons in the

concentrated area. As markers, **nanoparticulate** fillers-coated or uncoated-may be used for diagnosis of medical conditions. For example, fillers exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...by normal kidney action without the development of stones or other adverse side effects. While **nanoparticulates** may be removed naturally through kidney and other organs, they may also be filtered or removed externally through membranes or otherwise removed directly from blood or tissue. Carrier **nanoparticulates** may be reactivated externally through membranes and reused; for example, nutrient carriers may be removed...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed...

4/3,KWIC/54 (Item 19 from file: 654)
 DIALOG(R)File 654:US Pat.Full.
 (c) Format only 2006 Dialog. All rts. reserv.

0005780648 **IMAGE Available
 Derwent Accession: 2004-642005

INORGANIC DOPANTS, INKS AND RELATED NANOTECHNOLOGY

Inventor: Yadav, Tapesh, INV
 Alexander, John, INV

Correspondence Address: HOGAN & HARTSON LLP, ONE TABOR CENTER, SUITE
 1500 1200 SEVENTEENTH ST, DENVER, CO, 80202, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040170820	A1	20040902	US 2003455874	20030606
Division	US 6602595			US 2002150722	20020517
Division	US 6344271			US 99274517	19990323
Division	PENDING			US 2001790036	20010220
Division	US 6228904			US 9883893	19980522
Division	US 6202471			US 9874534	19980507
CIP	US 5905000			US 96739257	19961030
CIP	US 5952040			US 96730661	19961011
CIP	US 5851507			US 96706819	19960903
CIP	US 5788738			US 96707341	19960903
CIP	US 6513362			US 2001753806	20010103
Provisional				US 60-107318	19981106
Provisional				US 60-49077	19970609
Provisional				US 60-69936	19971217
Provisional				US 60-79225	19980324

Fulltext Word Count: 28433

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

- ...0114] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...
- ...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...
- ...0115] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...
- ...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...
- ...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...
- ...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...
- ...composition or with a phase that is compatible with the matrix composition. Such a coated **nanoparticle** is illustrated in FIG. 1, which shows a spherical **nanoparticle** 6 and a coating 8. In one embodiment, when embedding nanofillers in a polymer matrix...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

- ...0144] A **nanoparticulate** filler for biomedical operations might be a carrier or support for a drug of interest...
- ...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites may also have utility as markers or as carriers for markers. Their unique...
- ...0145] In some examples of biomedical functions, magnetic **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic **nanoparticles** can be utilized to carry drugs to region of interest and then photoactivated. Thermally sensitive **nanoparticles**

can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive **nanoparticulate** fillers may have utility for chemotherapy. **Nanoparticles** suitably doped with genetic and culture material may be utilized in similar way to deliver...

...in concentrating the particle and then providing the therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest using magnetic field, and finally activated using photons in the concentrated area. As markers, **nanoparticulate** fillers-coated or uncoated-may be used for diagnosis of medical conditions. For example, fillers...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...by normal kidney action without the development of stones or other adverse side effects. While **nanoparticulates** may be removed naturally through kidney and other organs, they may also be filtered or removed externally through membranes or otherwise removed directly from blood or tissue. Carrier **nanoparticulates** may be reactivated externally through membranes and reused; for example, nutrient carriers may be removed...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/55 (Item 20 from file: 654)

DIALOG(R) File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

0005720689 **IMAGE Available

Derwent Accession: 2004-543650

Non-specific sensor array detectors

Inventor: Steinthal, Gregory, INV

Sunshine, Steven, INV

Burch, Tim, INV

Plotkin, Neil, INV

Hsiung, Chang-Meng, INV

Assignee: Cyrano Sciences Inc.(02), Pasadena, CA

Correspondence Address: Foley & Lardner, 3000 K Street, N.W. Suite 500,
Washington, DC, 20007, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040135684	A1	20040715	US 2003624194	20030721
Provisional				US 60-397135	20020719

Fulltext Word Count: 15066

Description of the Invention:

...vapor based on the array pattern. The C320 has been successfully tested as a point **detector** for TICs (e.g., hydrazine, **ammonia**,

formaldehyde, ethylene oxide, insecticides) as well as CWAs (e.g., GA, GB, HN-3, VX...and are excellent ink jetting candidates. Other useful ink-jetting materials include surface modified gold nanoparticle formulations and nanotube formulations...

4/3,KWIC/56 (Item 21 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005714270 **IMAGE Available
Derwent Accession: 2004-569668
Nonotube-based electronic detection of biological molecules
Inventor: Star, Alexander, INV
Gruner, George, INV
Assignee: NANOMIX, INC.(02)
Correspondence Address: O'MELVENY & MYERS LLP, 400 South Hope Street, Los Angeles, CA, 90071-2899, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040132070	A1	20040708	US 2003704066	20031107
CIP	PENDING			US 2003656898	20030905
CIP	PENDING			US 2003345783	20030116
Provisional				US 60-424892	20021108
Provisional				US 60-408547	20020905
Provisional				US 60-349670	20020116

Fulltext Word Count: 4766
Summary of the Invention:

...carbon nanotubes have been found to be sensitive to various gases, such as oxygen and ammonia, and these observations have confirmed the notion that such devices can operate as sensitive chemical sensors.

[...]

...nanotubes grown on silicon or other substrates by chemical vapor deposition from iron-containing catalyst nanoparticles with methane/hydrogen gas mixture at 900 degree C. Other catalyst materials and gas mixtures

Description of the Invention:

...chemical vapor deposition (CVD) on 200 nm of silicon dioxide on doped silicon from iron nanoparticles with methane/hydrogen gas mixture at 900 degree C. Electrical leads may be patterned on...

...microscope (AFM) image of one of the devices after exposure to streptavidin labeled with gold nanoparticles indicated the presence of streptavidin. Based on the image, it appeared that streptavidin was effectively...

4/3,KWIC/57 (Item 22 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

0005705383
Derwent Accession: 2001-581203

Plasma-deposited coatings, devices and methods

Inventor: Zamora, Paul, INV

Tsang, Ray, INV

Chen, Meng, INV

Assignee: BioSurface Engineering Technologies, Inc.(02), College Park, MD,
US

Correspondence Address: PEACOCK MYERS AND ADAMS P C, P O BOX 26927,
ALBUQUERQUE, NM, 871256927

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040126596	A1	20040701	US 2003653655	20030902
Continuation	US 6613432			US 2000746234	20001221
Provisional				US 60-171844	19991222
Provisional				US 60-221646	20000728

Fulltext Word Count: 14057

Description of the Invention:

...devices, a variety of other implantable structures, such as wires, coils, sheets, pellets, particles, and nanoparticles, and the like, may be treated with the gas plasma containing molecular species composed of ...

...0134] Stainless steel surfaces treated in a glow discharge of ammonia alone, that is without oxygen, did not have any detectable N2, although a pronounced N1 peak was found...

4/3,KWIC/58 (Item 23 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

5658135

Derwent Accession: 2000-330097

Utility

CERTIFICATE OF CORRECTION

C/ High luster, flexible multilayered film with a polyamide outer layer containing nanodispersed filling material and utilization of said film for packaging foodstuffs

Inventor: Eggers, Holger, Freiburg, DE

Kaschel, Gregor, Bomlitz, DE

Assignee: Wolff Walsrode AG(03), Walsrode, DE

Wolff Walsrode AG DE (Code: 92978)

Examiner: Sergeant, Rabon (Art Unit: 171)

Assistant Examiner: Bissett, Melanie

Law Firm: Norris McLaughlin & Marcus

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6740422	A	20040525	US 2001807094	20010409
PCT	WO 200023508		20000427	WO 99EP7349	19991004
		371:			
		102e:			
Priority				DE 19847845	19981016

Fulltext Word Count: 6706

Summary of the Invention:

...material can optionally be stretched in order to achieve a still better orientation of the **nanoparticles**. Compared with those not containing nanoscale particles, such films exhibit a higher rigidity, a higher...

...a layer that is situated on the outside of the film with PA 6 containing **nanoparticles** are also described. All the structures mentioned have as an advantage a high oxygen barrier...

...6, such a film having the structure PA 6/(80% PA MXD6+20% PA containing **nanoparticles**)//PA 6 do not exhibit any appreciable improvement in transparency. Such structures containing a high...

Description of the Invention:

...diaz paper. The number of blue-black spots on the diazo paper produced by the **ammonia** and **detectable** after 15 min is assigned to the number of buckling breaks in the film portion...

4/3,KWIC/59 (Item 24 from file: 654)

DIALOG(R) File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

0005602596 **IMAGE Available

Derwent Accession: 2004-355294

Electronic sensing of biomolecular processes

Inventor: Gruner, George, INV

Assignee: The Regents of the University of California(02)

Correspondence Address: GATES & COOPER LLP HOWARD HUGHES CENTER, 6701 CENTER DRIVE WEST, SUITE 1050, LOS ANGELES, CA, 90045, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040067530	A1	20040408	US 2003431963	20030508
Provisional				US 60-378843	20020508

Fulltext Word Count: 8536

Summary of the Invention:

...0004] Alternative techniques proposed, such as using **nanoparticle** probes (see, e.g. T.A. Taton et al., Science 289, 1757 (2000); and J...

Description of the Drawings:

...their surface layer. The arrow indicates the electronic conduction path. FIG. 1C shows a semiconductor **nanoparticle** coated with another material, with the arrows indicating the electronic conduction path...

...provides a schematic of the nanotube field effect transistor (NTFET) that uses a network of **nanoparticles** as conducting channel. A polymeric functional layer, which coats the network, functionalized with a molecular...

...image of the polymer-coated and biotinylated NTFET after exposure to streptavidin labeled with gold **nanoparticles**

[

Description of the Invention:

- ...percolation threshold". Preferable elements for use with embodiments of the invention include nanowires, nanotubes, and **nanoparticles**, such as metal oxides. Preferable elements for use with embodiments of the invention further include...
- ...invention include compensation for buffer conductivity (e.g. same arrangement as above but without the **nanoparticle** network...
- ...0035] Illustrative **Nanoparticle** Network Fabrication...
- ...context of the embodiments of the invention disclosed herein, artisans will understand that the term "**nanoparticle**" includes bulk **nanoparticles**, such as oxide **nanoparticles**, cocoons, nanowires, nanofibres, nanotubes, bundles of nanotubes, fullerenes and the like...
- ...the invention disclosed herein, artisans will understand that the term "network" comprises a collection of **nanoparticles** as defined above, providing a conduction path between two electrodes. The conducting path dominantly includes the **nanoparticles** in close proximity to each other, with the current flowing from one **nanoparticle** to the other, to the next, etc. In certain embodiments of the invention, networks are...
- ...For example in embodiments of the invention, a network can include both semiconducting and metallic **nanoparticles**.
- [...]
- ...electronic devices where the sensing element is a continuous film and electronic devices with one **nanoparticle** element such as a nanowire or a nanotube. The disclosed architecture of the embodiments of...
- ...addition, there is no need for patterned catalyst, and may be for a structure where **nanoparticles** are present in one location and not present in others on the wafer. Yet another...
- ...size compatibility with proteins allowing protein selective immobilization. Yet another advantage is that as many **nanoparticles** act as the conducting element, statistical averaging will occur, strongly reducing the signal variation from...
- ...and detection electronics. Yet another advantage is that by virtue of the large number of **nanoparticles** involved, the structure is also "defect tolerant..."
- ...as sensing element but the art can be equally well applied to a collection of **nanoparticles**, in particular to nanotube networks of to ...Such devices have been found to be sensitive to various gases, such as oxygen and **ammonia**, and thus can operate as sensitive chemical **sensors**. The mechanism responsible for the change of device characteristic is thought to be a charge...
- ...chemical vapor deposition (CVD) on 200 nm of silicon dioxide on doped silicon from iron **nanoparticles** with methane/hydrogen gas mixture at 900 degree C.; electrical leads were patterned on top...
- ...microscope (AFM) image of one of the devices after exposure to streptavidin labeled with gold **nanoparticles** is shown in FIG. 5. Light dots represent gold **nanoparticles** (10 nm), and thus indicate the presence of streptavidin. Based on the image, we conclude...

...the nanotube conducting channel. (This assumes that, on the average, one streptavidin molecule per gold nanoparticle is attached to the nanotube ...

...According to an AFM image of the device (FIG. 5), there are about 100 gold nanoparticles, and approximately 100 protein molecules (assuming one protein per gold nanoparticle binding to the tube) in close proximity to the carbon nanotube. Combining these two numbers...

...the wafer is covered with patterned photoresist and is spin coated with growth promoter containing nanoparticles of iron encased within a mesoporous material [(a) Li, W. Z.; Xie, S. S.; Qian...

...0079] (15) Streptavidin is labeled with gold nanoparticles for the purpose of AFM imaging. Streptavidin (from Streptomyces avidinii, Sigma Chemicals) without gold labeling...

4/3,KWIC/60 (Item 25 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

5589434 **IMAGE Available
Derwent Accession: 2002-434812

Utility

REASSIGNED

C/ Processing and manufacturing methods enabled using non-stoichiometric nanomaterials

Inventor: Yadav, Tapes, Longmont, CO
Au, Ming, Longmont, CO
Miremadi, Bijan, Longmont, CO
Freim, John, Longmont, CO
Avniel, Yuval, Longmont, CO
Dirstine, Roger, Longmont, CO
Alexander, John, Longmont, CO
Franke, Evan, Longmont, CO

Assignee: NanoProducts Corporation(02), Longmont, CO
Nano Products Corp (Code: 61074)

Examiner: Le, H. Thi (Art Unit: 173)

Combined Principal Attorneys: Langley, Stuart T.Hogan & Hartson LLP

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 6713176	A	20040330	US 2001996471	20011127
Division	Pending			US 99274517	19990323

Fulltext Word Count: 14950

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle.

...

...A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/61 (Item 26 from file: 654)
 DIALOG(R) File 654:US Pat.Full.
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0005577491

Derwent Accession: 1999-166996

Polyhydroxyalkanoates for in vivo applications

Inventor: Williams, Simon, INV
 Martin, David, INV
 Gerngross, Tillman, INV
 Horowitz, Daniel, INV

Assignee: Metabolix, Inc.(02)

Correspondence Address: PATREA L. PABST HOLLAND & KNIGHT LLP, SUITE 2000,
 ONE ATLANTIC CENTER 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA,
 30309-3400, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20040053381	A1	20040318	US 2003642026	20030815
Division	US 6623749			US 2001819447	20010328
Division	US 6245537			US 9876198	19980512
Provisional				US 60-65921	19971117

Provisional	US 60-63501	19971024
Provisional	US 60-54289	19970731
Provisional	US 60-46211	19970512

Fulltext Word Count: 16773

Summary of the Invention:

...hydrogen peroxide. The latex may contain particles of any size, although the particles are preferably **nanoparticles** and/or microparticles. The latex particles may be crystalline or amorphous, but are more preferably...

Description of the Invention:

...film surface was washed with water, quenched with glycine and blocked with 0.1% gelatin. **Detection** with a strepavidin horseradish peroxidase conjugate and a chemiluminescent HRP **detection** solution demonstrated biotin modification of the surface. A PHO film without ammonia gas plasma treatment was used as a control and demonstrated no biotin modification under identical...

Non-exemplary or Dependent Claim(s):

...The method of claim 17 wherein the device is in the form of microparticles or **nanoparticles** .

...

...The device of claim 41 wherein the device is in the form of microparticles or **nanoparticles** .

4/3,KWIC/62 (Item 27 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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0005423492 **IMAGE Available

Derwent Accession: 2004-212649

Inorganic colors and related nanotechnology

Inventor: Yadav, Tapesh, INV

Correspondence Address: HOGAN & HARTSON LLP, ONE TABOR CENTER, SUITE 1500 1200 SEVENTEENTH ST, DENVER, CO, 80202, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20030207112	A1	20031106	US 2003449278	20030530
Division	US 6602595			US 2002150722	20020517
Division	US 6344271			US 99274517	19990323
Division	PENDING			US 2001790036	20010220
Division	US 6228904			US 9883893	19980522
Division	US 5905000			US 96739257	19961030
Division	US 6202471			US 9874534	19980507
CIP	US 5952040			US 96730661	19961011
CIP	US 5851507			US 96706819	19960903
CIP	US 5788738			US 96707341	19960903
CIP	US 6513362			US 2001753806	20010103
Provisional				US 60-107318	19981106
Provisional				US 60-49077	19970609
Provisional				US 60-69936	19971217
Provisional				US 60-79225	19980324

Fulltext Word Count: 30730

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0113] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0114] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period... composition or with a phase that is compatible with the matrix composition. Such a coated **nanoparticle** is illustrated in FIG. 1, which shows a spherical **nanoparticle** 6 and a coating 8. In one embodiment, when embedding nanofillers in a polymer matrix...

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0143] A **nanoparticulate** filler for biomedical operations might be a carrier or support for a drug of interest...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites may also have utility as markers or as carriers for markers. Their unique...

...0144] In some examples of biomedical functions, magnetic nanoparticles such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic nanoparticles can be utilized to carry drugs to region of interest and then photoactivated. Thermally sensitive nanoparticles can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive nanoparticulate fillers may have utility for chemotherapy. Nanoparticles suitably doped with genetic and culture material may be utilized in similar way to deliver...

...in concentrating the particle and then providing the therapeutic action. To illustrate, magnetic and photocatalytic nanoparticles may be formed into a composite, administered to a patient, concentrated in area of interest using magnetic field, and finally activated using photons in the concentrated area. As markers, nanoparticulate fillers-coated or uncoated may be used for diagnosis of medical conditions. For example, fillers...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that nanoparticulates can be released into the body in a controlled fashion over a long time period...

...by normal kidney action without the development of stones or other adverse side effects. While nanoparticulates may be removed naturally through kidney and other organs, they may also be filtered or removed externally through membranes or otherwise removed directly from blood or tissue. Carrier nanoparticulates may be reactivated externally through membranes and reused; for example, nutrient carriers may be removed...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a sensor or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/63 (Item 28 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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5371824

Derwent Accession: 1999-166996

Utility

C/ Medical device containing polyhydroxyalkanoate treated with oxidizing agent to remove endotoxin

; POLYLACTONES WHICH DO NOT ELICIT AN ACUTE INFLAMMATORY RESPONSE WHEN IMPLANTED INTO AN ANIMAL; TISSUE COATINGS, STENTS, SUTURES, TUBING, BONE AND OTHER PROSTHESES, BONE OR TISSUE CEMENTS, TISSUE REGENERATION DEVICES

Inventor: Williams, Simon F., Sherborn, MA

Martin, David P., Arlington, MA

Gerngross, Tillman, Cambridge, MA

Horowitz, Daniel M., Somerville, MA

Assignee: Metabolix, Inc.(02), Cambridge, MA

Metabolix Inc (Code: 37821)
Examiner: Naff, David M. (Art Unit: 161)
Law Firm: Holland & Knight LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6623749	A	20030923	US 2001819447	20010328
Division	US 6245537	A		US 9876198	19980512

Fulltext Word Count: 13564

Summary of the Invention:

...hydrogen peroxide. The latex may contain particles of any size, although the particles are preferably **nanoparticles** and/or microparticles. The latex particles may be crystalline or amorphous, but are more preferably...

Description of the Invention:

...film surface was washed with water, quenched with glycine and blocked with 0.1% gelatin. **Detection** with a streptavidin horseradish peroxidase conjugate and a chemiluminescent HRP **detection** solution demonstrated biotin modification of the surface. A PHO film without **ammonia** gas plasma treatment was used as a control and demonstrated no biotin modification under identical...

Non-exemplary or Dependent Claim(s):

...The device of claim 1 wherein the device is in the form of microparticles or **nanoparticles**.

4/3,KWIC/64 (Item 29 from file: 654)
DIALOG(R)File 654:US Pat.Full.
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5347237 **IMAGE Available
Derwent Accession: 2001-581203

Utility

C/ Plasma-deposited coatings, devices and methods
; PLASMA TREATMENT OF AN IMPLANTABLE MEDICAL DEVICE SURFACE WITH OF NITROGEN AND/OR OXYGEN MOLECULES, E.G., AMMONIA, NITROGEN OXIDE, OXYGEN ETC.; ANTICOAGULANTS, -INFLAMMATORY AGENTS; LESS RESTENOSIS, FIBROSIS

Inventor: Zamora, Paul O., Gaithersburg, MD

Osaki, Shigemasa, Sandy, UT

Chen, Meng, Salt Lake City, UT

Assignee: BioSurface Engineering Technologies, Inc.(02), College Park, MD
BioSurface Engineering Technologies Inc (Code: 59697)

Examiner: Nakarani, D. S. (Art Unit: 173)

Combined Principal Attorneys: Slusher, Stephen A.Peacock, Myers & Adams, PC

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6613432	A	20030902	US 2000746234	20001221

Fulltext Word Count: 10952

Description of the Invention:

...devices, a variety of other implantable structures, such as wires, coils, sheets, pellets, particles, and nanoparticles, and the like, may be treated with the gas plasma containing molecular species composed of ...Stainless steel surfaces treated in a glow discharge of ammonia alone, that is without oxygen, did not have any detectable N2, although a pronounced N1 peak was found...

4/3,KWIC/65 (Item 30 from file: 654)
DIALOG(R)File 654:US Pat.Full.
(c) Format only 2006 Dialog. All rts. reserv.

5331582 **IMAGE Available
Derwent Accession: 2002-617574

Utility

REASSIGNED

C/ Applications and devices based on nanostructured non-stoichiometric substances

Inventor: Yadav, Tapesh, Longmont, CO
Au, Ming, Longmont, CO
Miremadi, Bijan, Longmont, CO
Freim, John, Longmont, CO
Avniel, Yuval, Longmont, CO
Dirstine, Roger, Longmont, CO
Alexander, John, Longmont, CO
Franke, Evan, Longmont, CO

Assignee: NanoProducts Corporation(02), Longmont, CO
Nano Products Corp (Code: 61074)

Examiner: Le, H. Thi (Art Unit: 173)

Combined Principal Attorneys: Langley, StuartHogan & Hartson., LLP

	Publication Number	Kind	Date	Application Number	Filing Date
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Main Patent	US 6607821	A	20030819	US 2001996500	20011127
Division	US 6344271	A		US 99274517	19990323

Fulltext Word Count: 14936

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle.

...

...A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...In some examples of biomedical functions, magnetic non-stoichiometric nanoparticles such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric nanoparticles can be utilized to carry drugs to a region of interest and then photoactivated.

Thermally sensitive non-stoichiometric nanoparticles can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric nanoparticulate fillers are anticipated to have utility for chemotherapy. Nanoparticles suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

- ...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic nanoparticles may be formed into a composite, administered to a patient, concentrated in area of interest...
- ...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric nanoparticulate fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...
- ...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that nanoparticulates can be released into the body in a controlled fashion over a long time period...
- ...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a sensor or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/66 (Item 31 from file: 654)
DIALOG(R) File 654:US Pat.Full.
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5331540 **IMAGE Available
Derwent Accession: 2003-265856
Utility

C/ Nanotechnology for photonic and optical components

Inventor: Yadav, Tapes, Longmont, CO

Miremadi, Bijan, Longmont, CO

Assignee: NanoProducts Corporation(02), Longmont, CO

Nano Products Corp (Code: 61074)

Examiner: Le, H. Thi (Art Unit: 173)

Law Firm: Stuart Langley Hogan & Hartson, LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6607779	A	20030819	US 2002150201	20020517
Division	US 6344271	A		US 99274517	19990323

Fulltext Word Count: 14877

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle.

...

...A nanoparticulate non-stoichiometric filler for biomedical operations

might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/67 (Item 32 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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5316651 **IMAGE Available

Derwent Accession: 2003-438777

Utility

C/ Nanotechnology for inks and dopants

; INK COMPRISING: A NON-STOICHIOMETRIC NON-EQUILIBRIUM NANOSTRUCTURED MATERIAL; DEVICE SUCH AS ELECTRONICS USING SUCH A MATERIAL

Inventor: Yadav, Tapes, Longmont, CO

Au, Ming, Longmont, CO

Miremadi, Bijan, Longmont, CO

Freim, John, Longmont, CO

Avniel, Yuval, Longmont, CO

Dirstine, Roger, Longmont, CO

Alexander, John, Longmont, CO

Franke, Evan, Longmont, CO

Assignee: NanoProducts Corp.(02), Longmont, CO

Nano Products Corp
NanoProducts Corp (Code: 61074)
Examiner: Le, H. Thi (Art Unit: 173)
Combined Principal Attorneys: L, S TH & H

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6602595	A	20030805	US 2002150722	20020517
Division	US 6344271	A		US 99274517	19990323

Fulltext Word Count: 8908

Description of the Drawings:

- ...the filler may also be utilized as a means to time drug-release from a **nanoparticle** . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle** .
...
- ...A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...
- ...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...
- ...In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...
- ...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...
- ...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...
- ...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...
- ...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia** , hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/68 (Item 33 from file: 654)
DIALOG(R) File 654:US Pat.Full.
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5316599 **IMAGE Available
Derwent Accession: 2003-370705

Utility

C/ Nanotechnology for magnetic components

Inventor: Yadav, Tapesh, Longmont, CO

Au, Ming, Longmont, CO

Miremadi, Bijan, Longmont, CO

Freim, John, Longmont, CO

Avniel, Yuval, Longmont, CO

Dirstine, Roger, Longmont, CO

Alexander, John, Longmont, CO

Franke, Evan, Longmont, CO

Assignee: NanoProducts Corporation(02), Longmont, CO

Nano Products Corp

NanoProducts Corp (Code: 61074)

Examiner: Le, H. Thi (Art Unit: 173)

Combined Principal Attorneys: Langley, Stuart T.Hogan & Hartson, LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6602543	A	20030805	US 2002147835	20020517
Division	US 6344271	A		US 99274517	19990323

Fulltext Word Count: 14727

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle** . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle** .

...

...A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic

action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/69 (Item 34 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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0005239701 **IMAGE Available

Derwent Accession: 2003-140540

Magneitc- nanoparticle conjugates and methods of use

Inventor: Lee Josephson, INV

Ralph Weissleder, INV

J. Perez, INV

Correspondence Address: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20030092029	A1	20030515	US 2002165258	20020606
Provisional				US 60-296378	20010606

Fulltext Word Count: 24660

Magneitc- nanoparticle conjugates and methods of use

Abstract:

The present invention provides novel compositions of binding moiety-**nanoparticle** conjugates, aggregates of these conjugates, and novel methods of using these conjugates, and aggregates. The **nanoparticles** in these conjugates can be magnetic metal oxides, either monodisperse or polydisperse. Binding moieties can...

Summary of the Invention:

...0002] This invention relates to magnetic **nanoparticle** conjugates and methods of use...

...particle; their effects on water relaxation rate are unspecified and not relevant to their application. **Nanoparticles** do not respond to the weak, magnetic fields of hand held magnets...

...0009] In another example, WO 01/19405 describes the preparation and uses of magnetic **nanoparticles** with various biomacromolecules attached ...

...new magnetic conjugates and methods for their synthesis and use. Each conjugate comprises a magnetic **nanoparticle** linked to a binding moiety that specifically binds to a target in a sample, such...

...and, in some aspects of the invention, at least two populations of the binding moiety- **nanoparticle** conjugates. Each conjugate in a population has a plurality, e.g., two, three, four, or more, of a single type of binding moiety attached to a **nanoparticle**. The **nanoparticle** is composed of a magnetic metal oxide and one or more functional groups, e.g ...

...included, they contain functional groups that enable the binding moiety to be attached to the **nanoparticle** to form the conjugate. The polymer can be a natural polymer, a synthetic polymer, a...

...carboxy, amino, or sulfhydryl groups. In some embodiments, the binding moiety is attached to the **nanoparticle** through disulfide groups. The metal oxides can also be associated with non-polymer functional groups to form the **nanoparticles**.

[...]

...oxide contains superparamagnetic iron oxide crystals. The superparamagnetic character of the iron oxide of the **nanoparticle** makes it a potent enhancer of water relaxation rates, an enhancement that is altered when...

...invention features an aggregate including a plurality of conjugates, wherein each conjugate includes a magnetic **nanoparticle** linked to a binding moiety that specifically binds to a target molecule, to another binding...

...specifically bind to a target molecule, wherein each conjugate in the first population comprises a **nanoparticle** including a magnetic metal oxide (e.g., a superparamagnetic metal oxide) linked to a plurality...

...site on the target molecule, and wherein each conjugate in the second population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind...

...0024] These compositions can include conjugates that further include functional groups that link the **nanoparticles** to the binding moieties. The functional groups can be amino, carboxy, or sulfhydryl groups. Alternatively, the conjugates can further include a polymer associated with the **nanoparticles**, and wherein the functional groups are bound to the polymer and to the binding moieties...

...covalent bond or by a disulfide bond. For example, oligonucleotides can be attached to the **nanoparticles** by a single covalent bond at the 3' or 5' end of each oligonucleotide...

...between about 15 and 100 mM^[sup]-1 sec^[sup]-1. In particular embodiments, the **nanoparticle** is an amino-derivatized cross-linked iron oxide **nanoparticle**.

[...]

...0026] In another aspect, the invention features a conjugate including a

magnetic nanoparticle linked to a first binding moiety, wherein the first binding moiety includes a cleavage site...

- ...target molecule to form an aggregate, wherein each conjugate in the first population includes a nanoparticle that includes a magnetic metal oxide linked to a plurality of first binding moieties that...
- ...site on the target molecule, and wherein each conjugate in the second population includes a nanoparticle including a magnetic metal oxide linked to a plurality of second binding moieties that bind...
- ...are capable of forming an aggregate, wherein each conjugate in a first population includes a nanoparticle including a magnetic metal oxide linked to a first binding moiety, wherein the first binding...
- ...of a target molecule in a sample, by obtaining first and second populations of oligonucleotide- nanoparticle conjugates, wherein each conjugate in the first population includes a nanoparticle having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the nanoparticle ; and wherein each conjugate in the second population includes a nanoparticle having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the nanoparticle ; wherein the first and second oligonucleotides are each complementary to first and second portions of...
- ...in the other populations; preparing a mixture of the first and second populations of oligonucleotide- nanoparticle conjugates; obtaining a fluid sample; contacting the mixture with the sample under conditions that enable...
- ...as a nucleic acid or polypeptide) from a sample by obtaining a conjugate including a nanoparticle having a magnetic metal oxide linked by a cleavable bond (e.g., a reducible disulfide...
- ...purification of nucleic acids or materials hybridizing to nucleic acids. The conjugates can be oligonucleotide- nanoparticle conjugates having a reducible disulfide bond to couple the oligonucleotides to the nanoparticles , and as a result reducing agents can separate the oligonucleotides from the nanoparticles at a desired time. Materials bound to the oligonucleotide portion of these oligonucleotide nanoparticle conjugates, such as double-stranded nucleic acids, can be obtained by the use of reducing...
- ...nucleic acid in a plurality of samples, by obtaining first and second populations of oligonucleotide- nanoparticle conjugates, wherein each conjugate in the first population includes a nanoparticle having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the nanoparticle , and wherein each conjugate in the second population includes a nanoparticle having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the nanoparticle ; wherein the first and second oligonucleotides are each complementary to first and second portions of...
- ...in the other populations; preparing a mixture of the first and second populations of oligonucleotide- nanoparticle conjugates; obtaining a plurality of fluid samples; contacting a portion of the mixture with each

...

- ...the samples to hybridize to the first and second oligonucleotides of both populations of oligonucleotide- **nanoparticle** conjugates; and simultaneously obtaining the relaxation properties of the fluid in each of the plurality...
- ...administering to the subject at least one population of conjugates, wherein each conjugate includes a **nanoparticle** having a magnetic metal oxide linked to a binding moiety that specifically binds to the...
- ...levels of mRNA in cells using a mixture of populations of superparamagnetic oligonucleotide-iron oxide **nanoparticle** conjugates and MR imaging. When the conjugates react with a target, e.g., mRNA, the...
- ...array format. In yet another embodiment, the invention features a method in which the oligonucleotide- **nanoparticle** conjugates and an MR detector are used to determine the pattern of gene expression in

Description of the Drawings:

- ...scheme in which alkanethiooligonucleotides were reacted with N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) activated **nanoparticles** to form **nanoparticle** conjugates P1 and P2. P1 and P2 hybridize with complementary oligonucleotides followed by aggregation and magnetic relaxivity changes. Dithiothreitol (DTT) treatment breaks the bond between **nanoparticle** and alkanethiooligonucleotide...
- ...FIGS. 2A to 2D are images of test tubes illustrating the effect of incubating oligonucleotide- **nanoparticle** conjugates with oligonucleotides. From left to right, 2A: P1 and P2; 2B: P1, P2 plus...
- ...0048]FIGS. 3A and 3B are images of gel electrophoresis of a P1/P2/oligonucleotide **nanoparticle** precipitate. FIG. 3A shows a gel run in non-denaturing conditions. Lane 1: No DTT...
- ...of a turbid medium (INTRALIPID(R)) after a complementary oligonucleotide is added to an oligonucleotide **nanoparticle** conjugate mixture, P1 and P2. DTT was added after 180 minutes...
- ...with total RNA extracted from various cell lines. FIG. 9B is an image of the **nanoparticle** conjugates with lysed cells from WT or GFP+human glioma lysate two hours following hybridization...
- ...0055]FIG. 10A is a graph illustrating the incubation of anti-GFP-P1 **nanoparticle** conjugates with GFP or BSA protein resulting in a significant decrease in T2. FIG. 10B...

Description of the Invention:

- ...or polysaccharide) linked, e.g., covalently or non-covalently, to a magnetic, e.g., superparamagnetic, **nanoparticle**. The binding moiety causes a specific interaction with a target molecule (or, in some embodiments...

...0059] **Nanoparticles**

[...

...0060] **Nanoparticles** can be monodisperse (a single crystal of a magnetic material, e.g., metal oxide, such as superparamagnetic iron

oxide, per nanoparticle) or polydisperse (a plurality of crystals, e.g., 2, 3, or 4, per nanoparticle). The magnetic metal oxide can also comprise cobalt, magnesium, zinc, or mixtures of these metals...

...superparamagnetic compounds and magnetite, gamma ferric oxide, or metallic iron. Important features and elements of nanoparticles that are useful to produce the new conjugates include: (i) a high relaxivity, i.e...

...can be covalently attached, (iii) a low non-specific binding of interactive moieties to the nanoparticle , and (iv) stability in solution, i.e., the nanoparticles do not precipitate...

...0061] In all embodiments, the nanoparticles are attached (linked) to the binding moieties via functional groups. In some embodiments, the nanoparticles are associated with a polymer that includes the functional groups, and also serves to keep...

...0062] In other embodiments, the nanoparticles are associated with non-polymeric functional group compositions. Methods are known to synthesize stabilized, functionalized nanoparticles without associated polymers, which are also within the scope of this invention. Such methods are...

...0063] The nanoparticles have an overall size of less than about 1-100 nm. The metal oxides are...

...e.g., about 5 to 20 nm thick or more. The overall size of the nanoparticles is about 15 to 200 nm, e.g., about 20 to 100 nm, about 40 ...

...0065] Synthesis of Nanoparticles

[...]

...0066] There are varieties of ways that the nanoparticles can be prepared, but in all methods, the result must be a nanoparticle with functional groups that can be used to link the nanoparticle to the binding moiety...

...functionalized polymer or to non-polymeric surface-functionalized metal oxides. In the latter method, the nanoparticles can be synthesized according to the method of Albrecht et al., Biochimie, 80 (5-6...

...0068] In another embodiment, oligonucleotides are attached to magnetic nanoparticles via a functionalized polymer associated with the metal oxide. In some embodiments, the polymer is...

...made using oligonucleotides that have terminal amino, sulfhydryl, or phosphate groups, and superparamagnetic iron oxide nanoparticles bearing amino or carboxy groups on a hydrophilic polymer. There are several methods for synthesizing carboxy and amino derivatized-nanoparticles . Methods for synthesizing functionalized, coated nanoparticles are discussed in further detail below...

...0069] Carboxy functionalized nanoparticles can be made, for example, according to the method of Gorman (see WO 00/61191...

...salts are mixed together and are then neutralized with ammonium hydroxide. The resulting carboxy functionalized nanoparticles can be used for coupling amino functionalized oligonucleotides, see Table 1...

- ...0070] Carboxy-functionalized **nanoparticles** can also be made from polysaccharide coated **nanoparticles** by reaction with bromo or chloroacetic acid in strong base to attach carboxyl groups. In addition, carboxy-functionalized particles can be made from amino-functionalized **nanoparticles** by converting amino to carboxy groups by the use of reagents such as succinic anhydride...
- ...0071] **Nanoparticle** size can be controlled by adjusting reaction conditions, for example, by using low temperature during...
- ...0072] **Nanoparticles** can also be synthesized according to the method of Molday (Molday, R. S. and D...
...52(3):353-67, and treated with periodate to form aldehyde groups. The aldehyde-containing **nanoparticles** can then be reacted with a diamine (e.g., ethylene diamine or hexanediamine), which will...
- ...0073] Dextran-coated **nanoparticles** can be made and cross-linked with epichlorohydrin. The addition of ammonia will react with epoxy groups to generate amine groups, see Hogemann, D., et al., Improvement of MRI probes to allow efficient detection of gene expression Bioconjug. Chem. 2000. 11(6):941-6, and Josephson et al., "High...
- ...0074] Carboxy-functionalized **nanoparticles** can be converted to amino-functionalized magnetic particles by the use of water-soluble carbodiimides...
- ...0075] Avidin or streptavidin can be attached to **nanoparticles** for use with a biotinylated binding moiety, such as an oligonucleotide or polypeptide. See e...
- ...cells," Bioconjug. Chem., 1996, 7(3):311-6. Similarly, biotin can be attached to a **nanoparticle** for use with an avidin-labeled binding moiety...
- ...0076] In all of these methods, low molecular weight compounds can be separated from the **nanoparticles** by ultra-filtration, dialysis, magnetic separation, or other means. The unreacted oligonucleotides can be separated from the oligonucleotide- **nanoparticle** conjugates, e.g., by magnetic separation or size exclusion chromatography...
- ...0080] In certain embodiments, the binding moieties are oligonucleotides, attached to the **nanoparticles** using any one of a variety of chemistries, by a single, e.g., covalent, bond, e.g., at the 3' or 5' end to a functional group on the **nanoparticle** .
- [...
- ...of the new in vitro assay methods uses at least two populations of oligonucleotide magnetic **nanoparticles** , each with strong effects on water relaxation (see Table 2). As the oligonucleotide- **nanoparticle** conjugates react with a target oligonucleotide, they form aggregates (100-500 nm; aggregates were 215...
- ...the relaxation properties of the solvent, which are altered when the mixture of magnetic oligonucleotide **nanoparticles** reacts with a target nucleic acid to form aggregates...
- ...is the need for a mixture of at least two types of magnetic metal oxide **nanoparticles** , each with a specific sequence of oligonucleotide, and each with more than one copy of the oligonucleotide attached, e.g., covalently, per **nanoparticle** . The assay protocol involves preparing a mixture of populations of oligonucleotide- **nanoparticle** conjugates and

reacting the mixture with a target nucleic acid. Alternatively, oligonucleotide- **nanoparticle** conjugates can be reacted with the target in a sequential fashion. A second feature of...

...analytical method is the use of magnetic resonance to detect the reaction of the oligonucleotide- **nanoparticle** conjugates with the target nucleic acid. When a target is present, the dispersed conjugates self...

...synthesized by methods known in the art, and used in conjunction with an avidin-bound **nanoparticle** .

[...]

...Similar bifunctional conjugation reagents, such as SPDP and reacting with the amino group of the **nanoparticle** and thiol group of the polypeptide, can be used with any thiol bearing binding moiety...

...is low. For example, up to twenty 2 kDa peptides can be attached to a **nanoparticle** , calculated assuming 2064 iron atoms per **nanoparticle** . With larger binding moieties like proteins (generally greater than about 30 kDa) the same mass of attached polypeptide results in only approximately 1-4 binding moieties per **nanoparticle** . Second, polypeptides can be engineered to have uniquely reactive residues, distal from the residues required for biological activity, for attachment to the **nanoparticle** . The reactive residue can be a cysteine thiol, an N-terminal amino group, a C...

...or an ectodomain of a cell surface protein. In each case, the resulting binding moiety- **nanoparticle** is used to measure the presence of analytes in a test media reacting with the...

...a covalent bond, at one of the two ends, to a functional group on the **nanoparticle** . The polysaccharides can be synthetic or natural. Mono-, di-, tri- and polysaccharides can be used...

...osazones, sugar alcohols, sugar acids, sugar phosphates when used with appropriate attachment chemistry to the **nanoparticle** .

[...]

...0106] A generally useful method of accomplishing linking is to couple avidin to a magnetic **nanoparticle** and react the avidin- **nanoparticle** with commercially available biotinylated polysaccharides, to yield polysaccharide- **nanoparticle** conjugates. For example, sialyl Lewis based polysaccharides are commercially available as biotinylated reagents and will...

...0111] Coupling of Binding Moieties to **Nanoparticles** to Prepare Conjugates...

...0112] The conjugates are prepared by linking two or more binding moieties to each magnetic **nanoparticle** . A general procedure for synthesizing amino-cross linked iron oxide **nanoparticle** begins with the synthesis of a dextran coated superparamagnetic iron oxide. There are a variety...

...0114] Coupling of Oligonucleotides to **Nanoparticles**

[...]

...reactive 3', 5', or both termini. One terminus is attached to the surface of the **nanoparticle** , leaving the other terminus free for

attachment to another molecule, e.g., a biotin group...

...techniques and reagents that can be used to couple oligonucleotides to amino- or carboxy-functionalized **nanoparticles**. The general strategy is to provide an oligonucleotide with a unique reactive group on the...

...end are of particular value, and are commercially available. They can be coupled to amino- **nanoparticles** through the use of reagents such as N-succinimidyl 3-(2-pyridyldithio)propionate (SPDP) and long chain SPDP (1c-SPDP) that produce a cleavable disulfide bond between the **nanoparticle** and the oligonucleotide. Amino- **nanoparticles** can also be reacted with reagents such as succinimidyl-iodoacetate to produce non-cleavable bonds between the **nanoparticle** and oligonucleotide...

...0117] Thus, **nanoparticles** can be conjugated to oligonucleotides through a variety of conjugation chemistries. See U.S. Pat...

...0119] In other embodiments, populations of **nanoparticle** conjugates can be synthesized by allowing biotinylated oligonucleotides, polypeptides, or polysaccharides, to react with avidin (or streptavidin)-bound **nanoparticles**. Here a non-covalent, but tight, bond between the biotinylated binding moiety, e.g., oligonucleotide, and avidin of the **nanoparticle** attaches the oligonucleotide to the **nanoparticle**. Oligonucleotide- **nanoparticle** conjugate populations prepared in this fashion are analogous to those prepared with covalent chemistries (Table...

...the formation of aggregates and changes in T₂. In this case, two populations of oligonucleotide- **nanoparticle** conjugates are formed when the avidin- **nanoparticle** is reacted with two biotinylated oligonucleotides. An advantage of this indirect capture method is that...

...that react with a target oligonucleotide are far smaller, and hence react faster, than oligonucleotide- **nanoparticle** conjugates. Biotinylated-oligonucleotides have molecular weights less than 50 kDa, while oligonucleotide- **nanoparticle** conjugates have molecular weights greater than about 1000 kDa (e.g., 1000, 2000, 3500, 5000...

...0122] Coupling of Polypeptides and Antibodies to **Nanoparticles**

[...

...reactive 3', 5', or both termini. One end is linked to the surface of the **nanoparticle**, leaving the other end free for attachment to another molecule, e.g., a biotin group...

...0124] The conjugation of polypeptides to **nanoparticles** can be accomplished by a large number of conjugation chemistries and reagents some of which are also used for attaching oligonucleotides to **nanoparticles**, see Table 1. A preferred general strategy is to use one of the large number of bifunctional agents that can be reacted first with the amino group of the **nanoparticle**, and secondly with the thiol group of the polypeptide (or biomolecule). Examples of such bifunctional...

...The bifunctional agent is dissolved in DMSO and reacted in excess with the amino functionalized **nanoparticle** at pH 8 using a non-amine containing buffer (e.g., borate, phosphate). Unreacted bifunctional...

...Tat peptide conjugates, Bioconjugate Chemistry, 10, 186-91; Perez et al. (2002) DNA-based magnetic **nanoparticle** assembly acts as a magnetic

relaxation nanoswitch allowing screening of DNA-cleaving agents, Journal of...

...synthesized by allowing a biotinylated antibody or antibody fragment to react with avidin (or streptavidin) **nanoparticles**. Here a non-covalent, but tight, bond between the biotinylated antibody and avidin of the **nanoparticle** attaches the antibody to the **nanoparticle**.

[...]

...another embodiment, a natural or synthetic polypeptide is covalently or non-covalently attached to the **nanoparticle** while the other terminal is biotinylated...

...invention, both ends of the polypeptide are biotinylated and avidin is directly attached to the **nanoparticle**.

[...]

...another embodiment, both termini of the peptide are covalently or non-covalently attached to two **nanoparticles**.

[...]

...0129] Coupling of Polysaccharides to **Nanoparticles**

{...}

...for preparing polysaccharides with reactive ends. One end is attached to the surface of the **nanoparticle**, leaving the other end free for attachment to another molecule. For example, as described above...

...the polysaccharide can be biotinylated on both termini and exposed to avidin linked to a **nanoparticle**.

[...]

...contains 2 to about 20 (e.g., 3, 5, 7, 10, 15, or 20) individual **nanoparticle** conjugates held together by the interaction (e.g., binding) of the binding moiety with a target, or with another binding moiety. The association of the **nanoparticles** is mediated by the attached biomolecules and not by **nanoparticle** non-specific attractions. This aggregate is approximately 100-500 nm (e.g., 200, 250, 300...

...mesh. The size of the openings can be controlled by adjusting the size of the **nanoparticles** and the size of the binding moieties on each conjugate. The small aggregates are stable...

...cluster, which is, in effect, an aggregate of aggregates. The cluster contains greater than 20 **nanoparticles** and is greater than 500 nm in size. The cluster is not useful since it...

...0135] The **nanoparticle** conjugates can be used as magnetic nanosensors or magnetic relaxation switches (MRS) in various detection...

...non-degradable oligonucleotide analogs (e.g., peptide nucleic acid or PNA) may be coupled to **nanoparticles** and used to image sequences of nucleic acids in vivo. Nontoxicity is evident from the use of magnetic **nanoparticles** as the active ingredient of COMBIDEX(R), a **nanoparticle**-based MR contrast agent, which has been judged approvable by the FDA (January 1999). COMBIDEX the examples described herein consists of

monodisperse or polydisperse, fluid-phase **nanoparticles** containing superparamagnetic $\text{Fe}_{20}\text{Fe}_{30}$ (3-5 nm...

...hybridization conditions are established by methods well known in the art. Hybridization of the oligonucleotide- **nanoparticle** conjugates to the target nucleic acids is typically performed under moderate to high stringency conditions...

...varied to achieve the optimal level of identity between the base sequences of the oligonucleotide- **nanoparticle** conjugates and those of the target oligonucleotide or nucleic acid being detected. These techniques and...

...0144] The **nanoparticles** P1 and P2 are potent enhancers of the spin-spin and spin-lattice relaxation processes...

...0145] The effect of temperature cycling on the hybridization of the oligonucleotide **nanoparticle** was investigated by measuring changes in T2 values (FIG. 5). At 80[degree sign] C...

...representative T2 changes were observed. Furthermore, upon addition of DTT, oligonucleotides were cleaved from the **nanoparticles** and T2 did not change during further temperature cycling. These results indicate that oligonucleotide hybridization...

...0147] A unique feature of the magnetic **nanoparticles** is that they are highly stable to temperature fluctuations and to different ionic media. This...

...0152] Uses of Binding Moiety- **Nanoparticle** Conjugates...

...0159] First, HYRAS involves the assay of nucleic acids using superparamagnetic iron oxide **nanoparticles**, and is based on the observation that nucleic acids do not non-specifically adsorb to...

...contain a multiplicity of phosphate groups, do not interact non-specifically with the iron oxide **nanoparticles**.

[...

...0160] Second, to produce the needed aggregation of **nanoparticles** by a specific target nucleotide, two types of oligonucleotide- **nanoparticles** are needed, each with a single type of oligonucleotide attached, each reacting with a different...

...target complementary oligonucleotide (see FIG. 1). If two different oligonucleotides were coupled to the sample **nanoparticle**, the target nucleic acid would hybridize to the oligonucleotides on the same particle and no...

...4 of U.S. Pat. No. 5,164,297. In contrast, in HYRAS, when oligonucleotide- **nanoparticles** react with a target nucleotide to form aggregates there is a decrease in T2...

...gold based colorimetric assays described in WO 98/04740. In one method using the gold **nanoparticles**, the color change is determined in solution, which requires a non-turbid, non-opaque solution...

...In the present invention, neither separation nor amplification steps are used. Instead, the presence of **nanoparticle** aggregate is detected by

MR. The invention can be distinguished by the ability to "see...

- ...CLIO, as described herein. Alternatively, non-polymer coated iron oxide particles can be used. The **nanoparticles** are then coupled to specific oligonucleotides as shown, e.g., in FIG. 1. The resulting oligonucleotide- **nanoparticle** conjugates are then formulated in a physiologically acceptable media (e.g., saline or isotonic mannitol...
- ...the mRNA of interest and is bound at the 3' or 5' termini to the **nanoparticle** . A second conjugate is synthesized with a oligonucleotide sequence complementary to a different but proximate...
- ...below. Here a microtiter plate is prepared where each well contains different combinations of oligonucleotide- **nanoparticles** , i.e., combinations of oligonucleotides with different sequences attached to the same magnetic **nanoparticle** . The sequences of the oligonucleotides are chosen to permit hybridization, followed by aggregation and T2...
- ...in a sample. In this method, antibodies are linked covalently or non-covalently to the **nanoparticle** . To ensure that the antigen binding site is exposed, the C-terminus of the antibody or antibody fragment is attached to the **nanoparticle** . Monoclonal antibodies can be used for this method. A feature of this method is the need for a mixture of at least two types of **nanoparticles** , each with a specific binding moiety, e.g., monoclonal antibody attached. The antibodies are directed...
- ...0169] In another aspect of the invention, a polyclonal antibody can be attached to the **nanoparticle** . Since by definition these antibodies are multivalent, only a single population of conjugates is required...
- ...g., an antibody, in solution. In this assay, the antigen will be bound to the **nanoparticle** and placed into a sample. If an antibody directed to the antigen is present, binding...
- ...In another embodiment, the binding moiety can be a receptor-binding protein bound to the **nanoparticle** . When applied to a solution of cells, clustering of a cell surface receptor will result...
- ...A peptide sequence with a serine or tyrosine kinase recognition site is attached to a **nanoparticle** at one terminal end. Addition of a solution containing a kinase will result in the...
- ...target molecules in a sample solution. The assay is based on the attachment to the **nanoparticle** of a natural or synthetic peptide that has an internal enzymatic site. Biotin is attached...
- ...internal hydrolytic sequence can have biotin attached to both termini. Avidin is attached to the **nanoparticles** and mixed with the biotinylated peptide in a sample. Since one avidin molecule binds four...
- ...0179] In another aspect of the invention, immediate aggregation is induced by attaching a **nanoparticle** to both termini of the peptide. The conjugate is placed in the sample and the...
- ...can form a dam methylation site (GATC). The hybridization results in aggregation of the attached **nanoparticle** and a measurable decrease in T2. Upon contact with a methylase, the adenine and cytosine...
- ...endonuclease restriction site (e.g., EcoRI, BamHI, PvuII). Hybridization of the oligonucleotides also aggregates the **nanoparticles** attached to the oligonucleotides resulting in a decreased T2. In this case, the

presence of...

...Synthesis of Superparamagnetic Iron Oxide Nanoparticles

[...]

...0184] Biocompatible, fluid phase magnetic nanoparticles (NH₂-CLIO) were synthesized as described and reacted with N-succinimidyl 3-(2...

...Conjugation of Nanoparticles to Alkanethiol Oligonucleotide...

...Use of Nanoparticle Conjugates in Turbid Media...

...0192] Equimolar amounts in iron of oligonucleotide-nanoparticle conjugates denoted P1 and P2 were diluted in a 10% Fat Emulsion (Intralipid(R) 10...

...0193] Equimolar amounts in iron of oligonucleotide-nanoparticles denoted P1 and P2 were diluted with 1 M NaCl in 0.1 M sodium...

...because T2 drops. This is due to a hybridization-induced formation of aggregates between oligonucleotide-nanoparticle. No binding occurs with non-complementary targets, and thus, there is no change in T2...and the mixture was incubated for 3.5 hours at room temperature. The avidin-CLIO nanoparticle was separated from unreacted avidin using a magnetic separation column (Milttenyi Biotec, Auburn, Calif.). Iron...

...determined spectrophotometrically, and protein by the BCA method (Pierce). The number of avidins attached per nanoparticle was calculated using a molecular weight of 67 kDa for avidin and 2064 Fe atoms...

...0199] Avidin-CLIO nanoparticles made as described above were reacted with biotinylated polyclonal anti-GFP (Research Diagnostics Inc.) and...

...CGC-ATT-(CH₂)₃-SH (SEQ ID NO:17) were conjugated to nanoparticles as described in Example 3. The resulting conjugates (Magnetic Relaxation Switches, MRS), denoted P1 (AAT...

...After a one-hour incubation with BamHI, the aggregates were no longer present and monodisperse nanoparticle conjugates (50-60 nm) were observed instead (FIG. 12b...

...Protein Assay Using Monoclonal Antibody-Nanoparticle Conjugates...

...0206] Monoclonal antibodies can be coupled to polymer coated magnetic nanoparticles using a variety of chemistries (see, e.g., Weissleder et al., U.S. Pat. No...

...0207] In this assay format a P1 (first monoclonal attached to a nanoparticle) and P2 (second monoclonal attached to a nanoparticle) are synthesized in separate reactions. The target protein must contain epitopes for both monoclonals, so...

...in solution, the monoclonal antibodies will bind both epitopes on the antigen, thereby aggregating the nanoparticles, resulting in a decrease of T2...

Exemplary or Independent Claim(s):

1. An aggregate comprising a plurality of conjugates, wherein each conjugate comprises a magnetic nanoparticle linked to a binding

moiety that specifically binds to a target molecule, to another binding...

...specifically bind to a target molecule, wherein each conjugate in the first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of first binding moieties that bind ...

...site on the target molecule, and wherein each conjugate in the second population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind...

...36. A conjugate comprising a magnetic **nanoparticle** linked to a first binding moiety, wherein the first binding moiety comprises a cleavage site...

...target molecule to form an aggregate, wherein each conjugate in the first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of first binding moieties that bind ...

...site on the target molecule, and wherein each conjugate in the second population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a plurality of second binding moieties that bind...

...are capable of forming an aggregate, wherein each conjugate in a first population comprises a **nanoparticle** comprising a magnetic metal oxide linked to a first binding moiety, wherein the first binding...

...target molecule in a sample, the method comprising obtaining first and second populations of oligonucleotide- **nanoparticle** conjugates, wherein each conjugate in the first population comprises a **nanoparticle** having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the **nanoparticle** ; and wherein each conjugate in the second population comprises a **nanoparticle** having a metal oxide associated with a polymer having functional groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle** ; wherein the first and second oligonucleotides are each complementary to first and second portions of...

...in the other populations; preparing a mixture of the first and second populations of oligonucleotide- **nanoparticle** conjugates; obtaining a fluid sample; contacting the mixture with the sample under conditions that enable...

...purifying a target molecule from a sample, the method comprising obtaining a conjugate comprising a **nanoparticle** comprising a magnetic metal oxide linked by a cleavable bond to a binding moiety that...

...in a plurality of samples, the method comprising obtaining first and second populations of oligonucleotide- **nanoparticle** conjugates, wherein each conjugate in the first population comprises a **nanoparticle** having a magnetic metal oxide associated with a polymer having functional groups; and a plurality of first oligonucleotides attached to the functional groups on the **nanoparticle** , and wherein each conjugate in the second population comprises a **nanoparticle** having a metal oxide associated with a polymer having functional

groups; and a plurality of second oligonucleotides attached to the functional groups on the **nanoparticle** ; wherein the first and second oligonucleotides are each complementary to first and second portions of...

...in the other populations; preparing a mixture of the first and second populations of oligonucleotide- **nanoparticle** conjugates; obtaining a plurality of fluid samples; contacting a portion of the mixture with each...

...the samples to hybridize to the first and second oligonucleotides of both populations of oligonucleotide- **nanoparticle** conjugates; and simultaneously obtaining the relaxation properties of the fluid in each of the plurality...

...administering to the subject at least one population of conjugates, wherein each conjugate comprises a **nanoparticle** having a magnetic metal oxide linked to a binding moiety that specifically binds to the ...

Non-exemplary or Dependent Claim(s):

...The composition of claim 14, wherein the conjugates further comprise functional groups that link the **nanoparticles** to the binding moieties...

...The composition of claim 15, wherein the conjugates further comprise a polymer associated with the **nanoparticles** , and wherein the functional groups are bound to the polymer and to the binding moieties...

...25. The composition of claim 24, wherein the oligonucleotides are attached to the **nanoparticles** by a single covalent bond at the 3' or 5' end of each oligonucleotide...

...28. The composition of claim 14, wherein the plurality is three binding moieties per **nanoparticle** .

...

...35. The composition of claim 14, wherein the **nanoparticle** is an amino-derivatized cross-linked iron oxide **nanoparticle** .

4/3,KWIC/70 (Item 35 from file: 654)

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0005160630 **IMAGE Available

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Nanotechnology for chemical radiation, and biotechnology sensors

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Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle** . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle** .

[...]

...0088] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0089] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia** , hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/71 (Item 36 from file: 654)
DIALOG(R)File 654:US Pat.Full.
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0005160629 **IMAGE Available
Derwent Accession: 2003-330421
Nanotechnology for electrochemical and energy devices

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20030012952	A1	20030116	US 2002147599	20020517
Division	US 6344271			US 99274517	19990323
Provisional				US 60-107318	19981106
Provisional				US 60-111442	19981208

Fulltext Word Count: 15462

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle .

[...]

...0088] A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0089] In some examples of biomedical functions, magnetic non-stoichiometric nanoparticles such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric nanoparticles can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric nanoparticles can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric nanoparticulate fillers are anticipated to have utility for chemotherapy. Nanoparticles suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic

action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/72 (Item 37 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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0005125552 **IMAGE Available

Derwent Accession: 2003-438777

Nanotechnology for inks and dopants

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020176987	A1	20021128	US 2002150722	20020517
Division	US 6344271			US 99274517	19990323
Provisional				US 60-107318	19981106
Provisional				US 60-111442	19981208

Fulltext Word Count: 15566

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0088] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0089] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/73 (Item 38 from file: 654)

DIALOG(R) File 654:US Pat.Full.

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0005121391 **IMAGE Available

Derwent Accession: 2003-220201

Nanoscale catalyst compositions from complex and non-stoichiometric compositions

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020172826	A1	20021121	US 2002150140	20020517
Continuation	US 6344271			US 99274517	19990323
Provisional				US 60-107318	19981106

Fulltext Word Count: 15490

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a nanoparticle . A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the nanoparticle .

[...]

...0090] A nanoparticulate non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. Nanoparticulates and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0091] In some examples of biomedical functions, magnetic non-stoichiometric nanoparticles such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric nanoparticles can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric nanoparticles can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric nanoparticulate fillers are anticipated to have utility for chemotherapy. Nanoparticles suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic nanoparticles may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric nanoparticulate fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that nanoparticulates can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia , hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a sensor or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/74 (Item 39 from file: 654)
DIALOG(R) File 654:US Pat.Full.
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0005119158 **IMAGE Available
Derwent Accession: 2003-265856
Nanotechnology for photonic and optical components
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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020170593	A1	20021121	US 2002150201	20020517
Division	US 6344271			US 99274517	19990323
Provisional				US 60-107318	19981106
Provisional				US 60-111442	19981208

Fulltext Word Count: 15436

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0088] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0089] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic

action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, **ammonia**, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/75 (Item 40 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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0005117087 **IMAGE Available

Derwent Accession: 2003-120272

Nanotechnology for electronic and opto-electronic devices

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	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020168522	A1	20021114	US 2002147954	20020517
Division	US 6344271			US 99274517	19990323
Provisional				US 60-107318	19981106
Provisional				US 60-111442	19981208

Fulltext Word Count: 15447

Description of the Invention:

...the filler may also be utilized as a means to time drug-release from a **nanoparticle**. A polymer coating may further be used to enable selective filtering, transfer, capture, and removal of species and molecules from blood into the **nanoparticle**.

[...]

...0090] A **nanoparticulate** non-stoichiometric filler for biomedical operations might be a carrier or support for a drug...

...might even be the drug itself. Possible administration routes include oral, topical, and injection routes. **Nanoparticulates** and nanocomposites are anticipated to also have utility as markers or as carriers for markers...

...0091] In some examples of biomedical functions, magnetic non-stoichiometric **nanoparticles** such as ferrites may be utilized to carry drugs to a region of interest, where the particles may then be concentrated using a magnetic field. Photocatalytic non-stoichiometric **nanoparticles** can be utilized to carry drugs to a region of interest and then photoactivated. Thermally sensitive non-stoichiometric **nanoparticles** can similarly be utilized to transport drugs or markers or species of interest and then thermally activated in the region of interest. Radioactive non-stoichiometric **nanoparticulate** fillers are anticipated to have utility for chemotherapy. **Nanoparticles** suitably doped with genetic, cultured, or other biologically active materials may be utilized in a...

...assist in concentrating the particle and then providing therapeutic action. To illustrate, magnetic and photocatalytic **nanoparticles** may be formed into a composite, administered to a patient, concentrated in area of interest...

...activated using photons directed to the concentrated particles. As markers, coated or uncoated non-stoichiometric **nanoparticulate** fillers may be used for diagnosis of medical conditions. For example, fillers may be concentrated...

...magnetic resonance imaging or other techniques. In all of these applications, the possibility exists that **nanoparticulates** can be released into the body in a controlled fashion over a long time period...

...partially or completely, into a non-stoichiometric form by heat treating the device in borane, ammonia, hydrogen, methane, or silane to form a non-stoichiometric boride, nitride, oxide, hydride, carbide, silicide, or a combination thereof. In another example, a **sensor** or battery device can be prepared from stoichiometric electrochemical materials which can then be transformed

4/3,KWIC/76 (Item 41 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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0005113047 **IMAGE Available

Derwent Accession: 2003-247249

Nanotechnology for biomedical products

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Publication

Application

Filing